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SURGERY OF STENOTIC VALVULAR DISEASE OF THE HEART

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The past decade has seen the development of cardiac surgery assume a position of major importance, to climax a half century of far-reaching surgical achievement. For the most part, however, this surgery has been cardiovascular in nature and has been directed at the great vessels in close proximity to the heart (patent ductus arteriosus, coarctation of the aorta and anomalies of the aortic arch). Even when the vascular defects lay within the confines of the cardiac chambers (tetralogy of Fallot or mitral stenosis), newly developed familiarity with vascular anastomoses and an inborn dread of violating the sanctity of the heart itself suggested that indirect relief by vascular shunts might offer the most reasonable and effective solution. The brilliant successes of Gross,[1] Crafoord and Nylin,[2] Blalock[3] and Sweet[4] have been epochal in this regard, and their contributions cannot be overestimated.

Concomitantly with these essentially extracardiac developments, however, Smithy,[5] Harken and others,[6] Brock,[7] Murray, Wilkinson and McKenzie,[8] we ourselves[9] and others have been concerned with the development of intracardiac procedures designed for the relief of valvular disease and have focused attention on the direct cardiac approach; in so doing we have reaffirmed the right of cardiac surgery as a definitive entity.

Lest one be tempted to suspect that the conception of cardiac surgery is of recent origin, one has but to review the pioneer efforts of Rehn,[10] who successfully sutured a heart wound in 1897, Doyen[11] (1913), Tuffier[12] (1913), Allen and Graham[13] (1922), Souttar[14] (1925), Pribram[15] (1926), Cutler and Beck[16] (1929) and many others to appreciate that "true cardiac" surgery, initially handicapped by the immature state of surgical technic and anesthetic methods, nevertheless had its inception in the minds and actions of surgeons before many of us entertained the thought of embracing surgery as a specialty. Should valvular surgery of the heart in particular and intracardiac surgery in general become practical, and they have shown every indication of becoming just that, these men deserve a great measure of acclaim for their foresight; their contributions must not be forgotten in the enthusiasm of a presumably new and rapidly developing field.

It is logical that valvular disease of the heart should be among the first of the intracardiac disorders to be subjected to surgical consideration. It is common and found universally. Although the effects of rheumatic disease on the mitral and aortic valves make the acquired variety by far the commonest of all valvular defects, congenital stenosis of the pulmonary valve and conus as it occurs in the tetralogy of Fallot has received the greater attention to date due primarily to the ingenious systemic-pulmonary shunt devised by Blalock and Taussig.[17] As is well known, such an extracardiac shunt essentially by-passes the intracardiac pulmonary obstruction, redirecting mixed venous-arterial aortic blood into the pulmonary vascular bed where its oxygenation effectively relieves the clinical

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signs and symptoms manifested by the highly publicized "blue baby." Thus an additional (fifth) defect has been added to four already present in the tetralogy of Fallot, albeit one which in large measure overcomes the immediate and obvious effects of the condition under consideration. Nevertheless, a "patent ductus arteriosus" has been created, a defect which were it to be found in existence alone would demand early surgical correction. The late effects of such an arteriovenous fistula on the heart and circulation are well known, and although the interventricular septal defect in the tetralogy may conceivably counteract in some measure the deleterious late effects of an artificially produced ductus, there is certainly cause for real concern as to the eventual fate of a patient with such dangerous anomalies.

Without detracting in the least from the brilliant results achieved by the Blalock operation (subclavian artery–pulmonary artery anastomosis) or from its clever modification, the Potts operation [18] (direct aorta–pulmonary artery anastomosis), it would seem entirely reasonable to attempt direct relief of the pulmonary obstruction, thereby reducing (and not increasing) the number of defects with which the patient must contend. In order to effectively accomplish such an obviously desirable feat it is essential to thoroughly understand the nature of the obstruction in the pulmonary channel and to have perfected means of rapid, safe and efficient correction of this obstruction. Initial results of a direct surgical approach must be comparable to those already obtained by shunt procedures, and the prospect that the patient will have a more nearly permanent relief and a more certain future after undergoing operation by the direct method must at least theoretically outweigh present doubt which exists concerning the eventual physical havoc that may result from the presence of such a surgically-produced shunt.

CONGENITAL VALVULAR DISEASE

Pulmonary Stenosis.—Although a large number of cyanotic patients with various types of pulmonary obstruction have been studied clinically and treated surgically, there are few detailed data available as to the relative incidence of the individual anatomic variances which may be present within the right ventricular outflow tract or at the root of the pulmonary artery. It is well known, however, that pulmonary valvular stenosis may exist as a single defect or be found in association with any combination of intracardiac anomalies, particularly those designated by the term tetralogy of Fallot (pulmonary stenosis, overriding aorta, interventricular septal defect and hypertrophy of the right ventricle). To further complicate this picture the pulmonary stenosis component frequently may not be strictly valvular but rather infundibular, i. e., a muscular hypertrophy or fibrous malformation of the ventricular myocardium proximal to the pulmonary valve. As a result of this somewhat confused pathological pattern, it has been considered impractical to attempt definitive anatomic diagnosis of the type of pulmonary block but to be content with the compilation of functional or physiological data merely to confirm the presence of such an obstruction. Thus, for several years the demonstration of a greatly diminished pulmonary blood flow in a cyanotic child has called for the surgical production of a systemic-pulmonary shunt regardless of the type of obstruction.

18. Potts, W. J., and Gibson, S.: Aortic Pulmonary Anastomosis in Congenital Pulmonary Stenosis: Report of 45 Cases, J. A. M. A. **137**: 343 (May 22) 1948.

Mindful of the aforementioned objections to the creation of such a shunt, Brock [7] devoted considerable energy to a study of the pulmonary artery-conus segment in cyanotic heart disease in the hope that clarification might lead to a direct and logical surgical approach. His findings and subsequent conclusions are brilliant examples of the basic role played by exacting pathological observation in the development of any new surgical procedure. He has described the following variations: (1) pure valvular stenosis; (2) a high degree of pulmonary artery hypoplasia with a bicuspid valve and stenosis lying immediately subvalvular in a narrow muscular channel; (3) a high infundibular stenosis proximal to a relatively normal pulmonary artery and valve (the commonest type), and (4) a low infundibular stenosis, at varying levels, creating a small or large infundibular chamber (third ventricle) proximal to a normal pulmonary artery and valve. The wall of this chamber may be either thin and fibrous or muscular in nature (fig. 1).

As a result of these observations, Brock [7] in 1948 reported a new type of operation for the relief of congenital pulmonary stenosis. It is true that Doyen had previously attempted direct division of what was thought to be a stenosed pulmonary valve in 1913, but nothing further developed from this original effort. Inasmuch as pulmonary stenosis may be valvular or infundibular, two procedures were devised:

1. For relief of valvular stenosis entry is made through the right ventricle 3 cm. proximal to the valve. A small probe is inserted through the incision and passed into the mouth of the pulmonary artery to gage the position and degree of stenosis. A specially designed, flat, cobra-shaped knife with sharp cutting edges converging into a small noncutting rounded tip is guided into the fused valve cone, engaged through the tiny pinhole orifice and gently thrust onward into the pulmonary artery (fig. 2 *B*). The valve is thus divided into two equal cusps, one anterior and one posterior, which can open and close in response to changes in systolic and diastolic ventricular pressures. The knife is removed, a dilating sound or one's little finger is introduced through the opened valve to insure adequate separation of the newly formed cusps.

2. Should direct observation and palpation of the right ventricle and pulmonary artery at the time of surgical intervention suggest the presence of an infundibular type of obstruction, an alternative procedure is used. The ventricular chamber is entered either proximal or distal to the obstructing septum, and by means of a backward-cutting punch a collar of tissue is excised; this greatly enlarges the diameter of the outflow channel, allowing the venous blood stream to pass normally through the adequate pulmonary valve, artery and bed (fig. 2 *A*). In either case the ventricular incision is closed by using three or four interrupted sutures of strong vascular silk.

By 1949 Brock [19] was able to report that five cases of congenital pulmonary stenosis had been successfully treated by using the foregoing technic. Since that time he has operated on a much larger number of patients, both in this country in collaboration with Blalock and in England, with excellent results.

In December 1949, after prolonged deliberation and because of considerable experience obtained during the development of mitral valve surgery, we followed the suggestions of Brock and embarked on a course of direct pulmonary attack for routine cases of tetralogy of Fallot. Eight operations have been performed to date. Much to our surprise, a valvular stenosis was present in four of the eight patients, a much higher

19. Brock, R. C.: The Surgery of Pulmonary Stenosis, Brit. M. J. **2**: 399, 1949.

incidence than has been presumed to occur in this combination of defects. The ages ranged from 3½ years to 18, the fused valve cones were divided with strict adherence to the technic outlined above without undue incident, and in each instance the preoperative cyanosis has disappeared. In three patients the improvement in exercise tolerance has been striking, and the fourth patient has shown decided improvement but the operation was too recent to permit more adequate evaluation. Preoperative compensatory polycythemia has disappeared, peripheral arterial oxygen saturations have been greatly elevated in those so examined, and the low, directly measured pressures within the pulmonary artery before valvular division have risen to within normal range at the termination of the procedure (table 1).

In the four remaining cases the stenosis was infundibular, of the type shown in figure 1 *C*. Although in each instance the high location of the stenosis was suspected, the incision in the myocardium was inadvertently made directly over the infundibular septum, making the use of the Brock backward-cutting punch impossible. In the first of these infundibular cases (case 5) the condition of the patient at this point was so critical that digital and instrumental dilatation to

TABLE 1.—*Type of Stenosis and Surgical Result in Patients with Tetralogy of Fallot*

Case		Age (Yr.)	Type	Pulmonary Artery Pressure	
				Before	After
1	M. B.	3¼	Valvular	14.7	30.8 (mm. Hg)
2	H. C.	12½	Valvular	23.8	23.6 (mm. Hg)
3	R. B.	7	Valvular		Not taken
4	M. R.	18	Valvular	28	48 (cm. H_2O)
5	K. K.	2	Infundibular		Not taken
6	D. J.	4	Infundibular		Not taken
7	L. F.	8	Infundibular	25	31.5 (cm. H_2O)
8	A. S.	21	Infundibular		Not taken

forcibly enlarge the channel was all that could rapidly be accomplished so that the procedure could be terminated. Although there was no reason to believe that the child would survive the operation, after a stormy postoperative convalescence his improvement has been progressive, cyanosis has disappeared except with excessive exercise and the parents are delighted with the degree of normality which has been unexpectedly achieved. As a result of this experience, when the same problems were confronted in the ensuing three cases we were prepared with a small sharp bone rongeur with which a segment of septal tissue about 1.8 cm. (the size of a dime) was removed through the opening in the myocardium, an opening which extended vertically above and below the underlying septal ridge and at right angles to it (fig. 2 *C*). Each of these patients improved rapidly after operation. Cyanosis disappeared (immediately in one, within a few days in a second and after ten days in the third), and they have been discharged with decided improvement in their exercise tolerance.

Although it is obviously too early to draw any conclusions from this small series of cases (the longest postoperative observation is six months), certain generalizations are apparent. The direct ventricular approach to congenital pulmonary stenosis is entirely feasible. With application and a certain dispatch on the part of the operator, it can be done with a low mortality. There were no deaths in this series. The immediate and early results have been excellent, and without doubt our results have equalled and even surpassed those we obtained by the shunt procedures. It is mandatory, however, that enthusiasm for a new procedure be tempered by a consideration of the possible late complications which might arise to confound the enthusiast. A number of questions are unanswerable at present and must await the passage of time and further careful evaluation.

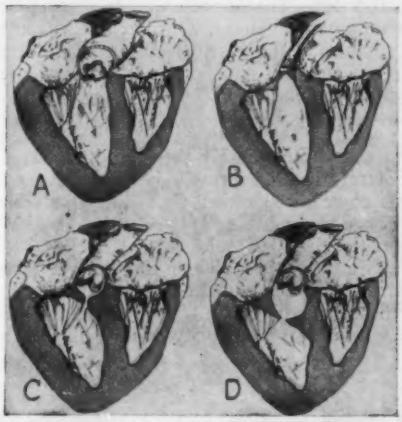

Fig. 1.—Types of pulmonary obstruction encountered in the tetralogy of Fallot: *A*, pure valvular stenosis; *B*, pulmonary artery hypoplasia with biscupid valve and subvalvular stenosis; *C*, high infundibular stenosis with normal valve, and *D*, low infundibular stenosis with normal valve. The other pathological components of the tetralogy of Fallot are not shown (*B*, *C* and *D*).

Does the direct division of a fused pulmonary valve by the method described produce appreciable regurgitation, and will the bicuspid nature of the cusps withstand the rigors of the continued and increasing ventricular output? Will such a valve be subject to the eventual deposition of bacterial thrombi as in subacute bacterial endocarditis? Will the newly formed cusps eventually fuse or the infundibular channel fibrose and contract? There are no data available to satisfactorily answer these obvious and most pertinent queries. Experiences with a somewhat similar type of procedure—in mitral stenosis—with a two and one-half year period of observation have shown that if early regurgitation is not appreciable its late development need not be feared; bicuspid valves can withstand much

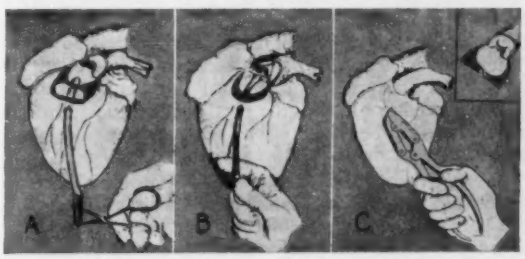

Fig. 2.—Methods for direct surgical relief of pulmonary obstruction in the tetralogy of Fallot: *A*, Brock punch in infundibular stenosis; *B*, Brock knife in valvular stenosis, and *C*, Glover rongeur in infundibular stenosis.

higher vascular pressures than are present in the right side of the heart; divided cusps which are constantly in action show little tendency to agglutinate in the absence of either insidious (rheumatic) or apparent infection when kept open by an almost constant vascular stream. The infundibular channel should not close for the same reasons provided an adequate amount of tissue has been

removed. No one can even postulate the probable incidence of superimposed bacterial infection. Suffice it to say that when one has the means to directly relieve congenital pulmonary stenosis and thereby not only to provide a more normal circulation but by such surgery to minimize or directly counteract in great measure the presence of the associated interventricular septal defect and overriding aorta, such possibilities must be explored to the uttermost. This is preferable to placing complete reliance on an added shunt, which at best is contrary to the very nature of the vascular system it is designed to improve. Complete data on cases briefly described herein are given elsewhere.[20]

ACQUIRED VALVULAR DISEASE

In the near future by far the greatest field of intracardiac surgical endeavor will be concerned with the problems of acquired rather than congenital disease, a mirror image of conditions as they exist today. White [21] has estimated that 0.5 to 1 per cent of the community at large is affected by valvular disease, particularly in those areas where rheumatic fever is endemic, as in the northeastern part of the United States and northern Europe. In the great majority of persons afflicted with

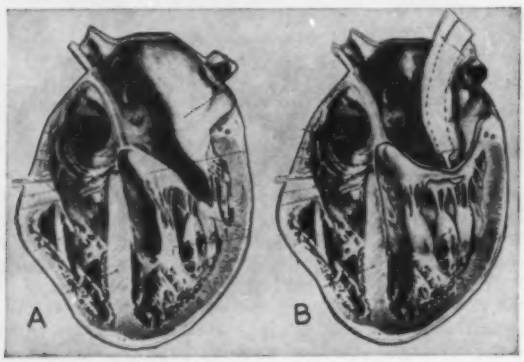

Fig. 3.—Sagittal sections through the heart showing the normal mitral valve (*A*) and diagrammatically the mitral valve in stenosis (*B*). The right index finger bearing the commissurotomy knife has been inserted through the left auricular appendage and the hooked blade engaged on the lateral commissure.

rheumatic heart disease (up to 85 per cent) there develops some degree of deforming valvular damage, the mitral and aortic valves being the commonest sites of involvement. Structural stenosis of these valves is the most serious result of rheumatic infection. It is little wonder, therefore, since stenosis is essentially a mechanical stricture, that surgical intervention should be considered as offering the ideal therapeutic approach provided it can be accomplished with relative safety and without the production of deleterious side effects.

Mitral Stenosis.—The prognosis of an individual case of mitral stenosis depends on many factors: the age of the patient; the severity of the lesion; the presence or absence of other valve defects; the presence or absence of additional rheumatic activity, and the condition of the myocardium. The ultimate outcome, however, is almost invariably unfavorable once the stenotic change gives rise to a progressive pattern. When the diagnosis of early mitral stenosis has been established, the cardiologist can picture and predict with considerable accuracy, by both repeated physical examination and observance of the patient's general condition, the structural and symptomatic phases through which a given patient will pass. Treatment by the cardiologist will at once be directed toward the prevention of further rheumatic insults and the support of a myocardium which is vainly attempting to maintain an adequate systemic circulation in the face of an increasing mechanical structure. In such circumstances both the cardiologist and the myocardium are fighting a losing battle. Doubtless just such reasoning prompted Sir Lauder Brunton [22] as early as 1902 to conclude that direct surgical incision of the stenotic valve provided the only logical method of interrupting the relentless chain of events in progressive mitral stenosis. Support of the myocardium by intelligent therapy has offered the only approach to date, but it is treatment of the effects of disease rather than alleviation of its mechanical cause. The ideal approach would be the elimination of the causative agent, rheumatic fever. Failing this, however, the correction of its disastrous cicatricial end result seems most logical.

Since the first section of the mitral ring by Cutler and Levine [23] in 1923 there have been a number of direct attacks on the stenotic mitral valve. The approach and the methods employed have varied. The left auricular appendage,[24] the left ventricle [25] and the left pulmonary vein [6] have been used as sites of entrance. Methods of dealing surgically with the valve have included simple incision of a valve cusp, excision of a portion of the mitral ring, digital dilatation of the stenotic orifice and valvuloplasty designed to resect portions of the valve ring at the commissures of the valve. A complete discussion of the merits and disadvantages of these many approaches and methods has been presented elsewhere.[9b, c] In summary, use of the left auricular appendage as the avenue of approach to the mitral valve is far superior to any other technic. Further, the aforementioned methods of valvular attack were based on the premise that the only hope of relieving the effects of mitral stenosis was to replace it by a regurgitant type of lesion. That this concept was erroneous has been shown repeatedly both in the experimental laboratory [26] and clinically, and to this concept we are unequivocally opposed. Of the approximately 24 patients so treated and recorded in the literature, 14 died promptly and the early survivors were so little improved that the majority succumbed in a relatively short time from their suddenly produced mitral regurgitation—a lesion equally as serious as the original stenosis, at least when produced surgically. We have employed the procedure of commissurotomy—a method in which the individual anatomic valve leaflets are surgically separated—to restore a considerable degree of valve function without the production of additional significant regurgitation. For a complete understanding of the basic principles underlying this surgical maneuver it is necessary to consider briefly the ana-

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24. Allen and Graham.[13] Souttar.[14]

25. Cutler, E. C.; Levine, S. A., and Beck, C. S.: The Surgical Treatment of Mitral Stenosis: Experimental and Clinical Studies, Arch. Surg. **9**(pt. 2): 689 (Nov.) 1924. Smithy.[5] Pribram.[15]

26. Powers, J. H.: Experimental Production of Mitral Stenosis, Arch. Surg. **18**: 1945, (April) 1929; Experimental Cardiac Valvular Disease in Dogs, and Subacute and Chronic Cardiac Valvular Disease in Man: Comparative Pathologic Study, ibid. **21**: 1 (July) 1930; Surgical Treatment of Mitral Stenosis: Experimental Study, ibid. **25**: 555 (Sept.) 1932. Cutler and Beck.[10]

tomic, pathological, and physiological aspects of the mitral valve as it appears normally and in its diseased state.

The normal mitral valve may be likened to a truncated cone of thin, flexible membrane. Its base is attached at the left atrioventricular ring, and its apex extends into the left ventricle. The apex and the outer surface of the apical half of this cone are suspended by numerous guy wires (chordae tendineae) attached to papillary muscles arising from the ventricular wall near the ventricular apex. The chordae tendineae are grouped more heavily in two areas of the mitral apex, at either side. These areas represent both the anatomic fusion of the two components of the valve (an anteromedial and a posterolateral leaf) and the corners of the apex on which the leaves fold themselves (fig. 3*A*). When modified by rheumatic disease, these points of folding become the "commissures." The plane of flattening is oblique (with the patient in the supine position), running from the left anterolateral portion of the valve posteromedially. The anterior or anteromedial valve cusp is larger than the posterolateral; it is continuous with the posterior portion of the intracardiac aortic wall. During auricular systole the posterior or posterolateral cusp lies well away from the ventricular wall. During ventricular systole the ventricular wall may approximate and support it. Thus mitral regurgitation is primarily a defect or dysfunction of the anteromedial valve cusp. A defect of the posterolateral cusp produces limited regurgitation rather than an uncontrolled reflux of blood, as seen when a defect in the continuity of the anteromedial cusp prevents normal deflection of the ventricular output into the intracardiac aorta. The papillary muscles contract synchronously with the ventricle, drawing the chordae tendineae taut, thus preventing the valve leaflets from becoming inverted or displaced backward into the auricle.

In rheumatic disease the mitral valve develops numerous minute cauliflower-like vegetations (1 to 2 mm. in diameter) in a row along the line of closure of the valve. Healing leads to the formation of scar tissue. With repeated infection and healing there is gradual development of fibrosis, thickening, and narrowing and shortening of the apical portion of the valve cone. This scarring and narrowing may be very limited in extent and may resemble merely a purse-string puckering of the valve orifice. In other instances the disease involves one fourth to three fourths of the cone, leaving a flexible margin along its base (fig. 4). In far-advanced disease the whole valve becomes a rigid, completely inflexible, often calcified structure resembling a hard, ovoid plaque surrounding a small fish-mouth slit. Most physicians, and even many pathologists, think of such extreme deformity as classic and the rule in mitral stenosis. We have found this condition in only five of our 50 cases.

Usually mitral rheumatic disease hardens or fixes the apex of the mitral cone in the infolded or flattened position so that the commissures become an anatomic reality. Thus stenosis is produced, offering pronounced resistance to the passage of blood from the left auricle into the left ventricle. Some degree of regurgitation through the mitral slit during ventricular contraction is common. Not infrequently mitral rheumatic disease hardens and shortens the valve cone to a point where the leaves cannot be approximated. Such cases of predominant mitral regurgitation are less common than those predominantly stenotic and at the present time are not amenable to surgical correction.

Mitral stenosis of any degree interferes with the filling of the left ventricle and with the maintenance of normal systemic cardiac output. Many hearts with mitral stenosis are unable to increase their output over and above resting body requirements. Any appreciable amount of work will quickly cause patients with this condition to become fatigued or dizzy and even momentarily to lose consciousness. Concurrently, since the egress of blood from the left auricle is impaired, increased pressure within and great dilatation of this chamber results. The high intra-auricular pressure is transmitted to the entire pulmonary vascular system and thence to the right ventricle (fig. 5). A chronic pulmonary hypertension ensues, with nocturnal or exertional pulmonary edema (dyspnea), rupture of pulmonary capillaries (hemoptysis) and failure of the right side of the heart (enlarged liver, ascites and peripheral edema).

Commissurotomy: As previously stated commissurotomy, a term suggested to us by Dr. Thomas Durant of Philadelphia, is the procedure we have employed to reestablish a pronounced degree of normal mitral valve function. Our present operative technic is simple and direct. It has been described in detail in previous publications.[27]

Commissurotomy consists of an operative approach through the left posterolateral chest wall with the patient in the right lateral position. The pericardium is incised longitudinally 1 cm. anterior or posterior to the phrenic nerve. The auricular appendage, usually distended but occasionally of normal size or even contracted, now protrudes from the pericardial sac. A purse-string suture of heavy braided silk is passed about the appendage at its base. A noncrushing clamp is closed over the base of the appendage, and a generous portion of its tip is amputated. Two gloves are worn on the operator's right hand. The blade of the commissurotomy guillotine knife is inserted between the gloves on the index finger (the tip of the outer glove has been removed and an opening made at the base of the index finger), and the finger is inserted into the left auricle as the clamp is released and as the purse-string suture is drawn taut about the finger. The finger is well tolerated by the auricle and causes no disturbance to the circulating blood. The valve is quickly and easily located. Its structure can readily be appreciated; the size of the orifice and the location of the commissures are determined. The knife is now protruded through the opening and the hooked blade engaged on the anterolateral commissure (fig. 3*B*). A backward stroke with the left hand on the knife handle or approximation of the guillotine blade usually divides the commissure adequately the first time. The finger again palpates the opening and gently dilates it. If the cut in the commissure does not extend well into normal valve tissue through the fibrotic ring, another cut is made under direct digital guidance. In patients who have a rather soft valve orifice decidedly diminished in cross-sectional area, simple opening of the lateral commissure is sufficient. In patients with a rigid, fixed and sometimes calcified valve, incision of the medial commissure also may be necessary. This is accomplished by pronating the hand, engaging the medial commissure and repeating the maneuver already described.

Fig. 4

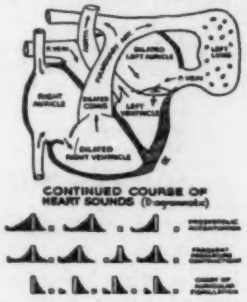

Fig. 5

Fig. 4.—Pathological conditions in late mitral stenosis. Note the decided fibrosis (possible calcific deposits) of cusp margins, extensive fusion of valve commissures, papillary muscles and chordae tendineae decidedly hypertrophied and contracted, and the pronounced dilatation of the left auricle, with early hypertrophy of the right ventricle. In the cross section of a stenotic valve note the induration along cusp margins, with the base of the valve relatively normal.

Fig. 5.—Physiological representation of cardiopulmonary vascular changes in mitral stenosis, showing the continued course of heart sounds and the progressive changes as seen in early adult life.

The finger and knife are now withdrawn from the auricle as the purse-string suture is tied securely, preventing loss of more than a few cubic centimeters of blood. The cut edge of the appendage is oversewn and the lumen of the appendage obliterated. There should be no disturbance of the systemic circulation and few, if any, circulatory irregularities throughout the procedure.

27. Footnote 9b, c and d.

Such a technic has the great advantage of direct digital guidance. It should not produce any significant amount of regurgitation because a considerable measure of valve function has been restored to prevent the reflux of blood during ventricular systole. That it effectively accomplishes the desired result is shown not only by decided clinical improvement but also by objective physiological studies. An abstract of the early cases in which this technic was used has appeared in previous communications.[9a, b]

Results: Commissurotomy by the technic described has been performed in 50 cases with eight fatalities (table 2). In the first of these a modified scalpel was employed, as our present hooked knife and guillotine modifications had not been perfected. Attempts to incise the commissures were attended by repeated disengagement of the blade as it rode over the fibrotic valve, resulting in an inadequate incision extending only a few millimeters into the scar tissue. The patient died on the sixth postoperative day in pulmonary edema from unrelieved mitral stenosis. Death occurred in cases 4 and 5 at a time when the proper technic for the management of the auricular appendage was being perfected. One patient died on the eighth postoperative day from a cerebral embolus originating in the unobliterated lumen prior to the routine use of a purse-string ligature at the base of the appendage. The other succumbed within twenty-four hours from hemorrhage through the purse-string ligature (mass ligature) before the importance of simultaneous obliteration and oversewing of the cut tip of the appendage was appreciated. Since the incorporation of these two steps into our surgical routine further disasters of this kind have not occurred.

TABLE 2.—*Commissurotomy for Mitral Stenosis, Mortality June 1948 to June 1950*

Year	Number of Cases	Number of Deaths
1948	5	3 (60%)
1949	21	3 (14.2%)
1950	24	2 (8.3%)*
Total	50	8 (16%)

* One by digital fracture of obstructive tissue and not the recommended incisional commissurotomy.

The five remaining fatalities all resulted from inadvertent but improper management of the valve itself and may be attributed for the most part to the production of immediately recognizable regurgitation at the time of surgical intervention; such regurgitation may be rapidly fatal, as in cases 26 and 44, in which death occurred within three hours as a result of an extensive tear just anterior to the lateral commissure caused by digital fracture of the obstructive tissue. The usual commissurotomy incision with the guillotine could not be made because the small size of the auricular appendage would not admit both finger and knife—a rare condition. The deleterious effects of acute regurgitation may be more prolonged and may be clinically manifest by the shocklike picture of peripheral vascular collapse. In case 10 the patient succumbed after four days in such a state despite intensive treatment designed to combat the usual shock syndrome. The two remaining fatalities (cases 36 and 16) occurred after three and four weeks, respectively, from relentless and increasing cardiac failure. In case 36 tearing occurred across the posterior cusp just posterior to the lateral commissure as traction was being made. In case 16 the mitral orifice was eccentrically placed and there was no lateral commissure; this necessitated a long medial incision—a dangerous and in this instance fatal procedure. One additional patient (case 14) contracted a severe upper respiratory infection involving the paranasal sinuses initially. All known antibiotics were used without effect. Bronchopneumonia developed, and death occurred in one month from overwhelming infection. This patient had enjoyed four postoperative months of freedom from the crippling effects of her previous mitral stenosis prior to this disaster. Her case is not listed as an operative mortality. Unfortunately, permission for an autopsy was not granted.

Forty-one patients on whom commissurotomy was performed are living and well at the present time. Twenty of these are considered to have excellent results based on the clinical disappearance of all presenting symptoms in each instance, the physiological demonstration of reduced pulmonary vascular pressures in many and the reduction of left auricular and over-all heart size in the majority. Twenty-one are improved according to these criteria. Five of this group had valves so severely damaged and distorted as to be considered essentially inoperable, and little return of valve function could be obtained although the valve orifices were partially opened. Obviously extensive improvement cannot be expected in these patients and their course, initially surprisingly good, will eventually be unsatisfactory. The remaining 16 patients may well continue to improve, as sufficient time has not elapsed in most instances for maximum benefit to have been derived.

Criteria for Selection of Candidates for Commissurotomy: The indications and contraindications for commissurotomy must be considered together. Both must change as experience dictates. The following criteria for the selection of cases have been recommended by Dr. George Geckeler, chief of cardiology, Hahnemann Medical College and Hospital, whose preparation and postoperative care of these patients has contributed immeasurably to the success of this surgical venture:

Most Favorable

1. Patient below age of 40.
2. Normal sinus rhythm and a presystolic accentuation of a late mitral diastolic murmur.
3. Systolic murmur, if any, of minimal intensity.
4. Pulmonic second sound accentuated not more than 1 plus.
5. No previous hemoptysis and no previous failure.
6. A good response to exercise tolerance test.
7. Right axis deviation and no left ventricular enlargement.

Less Favorable

1. Patient below age of 45.
2. Auricular fibrillation and a midlate decrescendo diastolic murmur.
3. Pronounced left auricular enlargement with moderate right ventricular enlargement.
4. Fair response to exercise tolerence test.
5. Electrocardiogram may show some T wave change indicative of myocardial damage.
6. No history of previous failure.

Least Favorable

1. Patient below age of 50.
2. Auricular fibrillation with a late decrescendo diastolic murmur.
3. A short, not more than grade 2, rough systolic murmur.
4. Two plus accentuation of the pulmonic second sound.
5. Fair to poor response to exercise tolerance test.
6. Previous failure should have been readily controlled.
7. Embolic phenomena may have been present.

8. There should be no more than minimal mitral insufficiency as shown physiologically by pressure curves and roentgenologically by little increase in size of left ventricle.

Inoperable

1. Patient above age of 50, except in rare instances.
2. Active rheumatic state.
3. Presence of unremedial failure or gallop rhythm or recent pulmonary infarction.
4. Aortic valve involvement of significant degree.
5. Appreciable degree of left ventricular enlargement.

Comment: It may be stated that in a case otherwise suitable for mitral commissurotomy, not infrequently the presence of recent and recurring arterial embolic phenomena is an urgent indication for surgical intervention. Ligation of the left auricular appendage has completely curtailed the recurrence of such episodes in 15 cases in this series. There was but one death (unrelated to embolism) in this group, and it has been unnecessary to give patients anticoagulants at any time during the postoperative period. As previously suggested,[9b] it may well be that surgical obliteration of the auricular appendages will prove to be the proper approach to the management of systemic or pulmonary embolization in many cases of auricular fibrillation unassociated with mitral stenosis.

Long term follow-up alone can supply the ultimate answer to the effectiveness of commissurotomy. From observations over the past two and one-half years it may be stated that surgery would appear to have an increasingly prominent place in the treatment of mitral stenosis and at the present time offers the only definitive solution to the problem.

Aortic Stenosis.—Emboldened by a reasonable measure of success with the surgical alleviation of stenosis of the mitral and pulmonary valves, it was natural that attention should be turned toward their counterpart in the aortic valve. Interest in this phase of valvular surgery was initiated by the enthusiasm and efforts of the late Horace Smithy, whose untimely death resulted from the rapid devastation of the diseased valve under discussion. It became apparent at once that the lessons learned and the approaches employed in the development of previous intracardiac surgical technics could not be transposed to the aortic valve because of the latter's variances in anatomic structure and relationship to vital coronary pathways. Nevertheless, certain broad patterns for investigation suggested themselves as a result of experiences encountered in this earlier experimental and clinical phase of valvular surgery.

Pathological and Physiological Considerations: The pathological basis of aortic stenosis is varied and complex. It appears that the primary defect in the rheumatic type is an early fusion of the three valve cusp margins. The free edges of the valve cusps are thickened, rolled and eburnated (fig. 6 A, insert). They may frequently contain calcium, but even in its absence they are extremely hard and tough. The valve leaflets themselves vary greatly but invariably are thickened and in most fixed specimens appear rigid and unyielding. In extreme cases the entire aortic valve may be considered as a rigid orifice surrounded by a calcified plaque that has lost all semblance of its original tricuspid nature. The fresh specimen, however, usually reveals a considerable amount of flexibility of the cusps themselves, especially near their attachments to the aortic wall. In this respect the pathologic condition resembles that found in the average case of mitral stenosis.

The disturbed physiological condition in extreme aortic stenosis is apparently due to the slow ejection of a small amount of blood with each contraction of the left ventricle. As a result the systolic blood pressure does not reach high levels but is sustained and maintained longer than is usual. Diastolic pressures likewise are relatively high, so that the pulse pressure differential is small. Coronary flow seems reduced more by the diminished volume of blood in the aorta than it is either by pressure changes or by intrinsic disease in the coronary system. Naturally, the coronary vascular needs of the left ventricle are increased by the large bulk of musculature contracting partly isometrically against the aortic obstruction. This extra work load increases the relative inadequacy of the coronary flow and partially explains the anginal or coronary type of pain so often encountered in these cases.

Patients with uncomplicated aortic stenosis are not primarily dyspneic unless congestive failure has supervened. They become progressively disabled as their cardiac stroke output diminishes with increasing

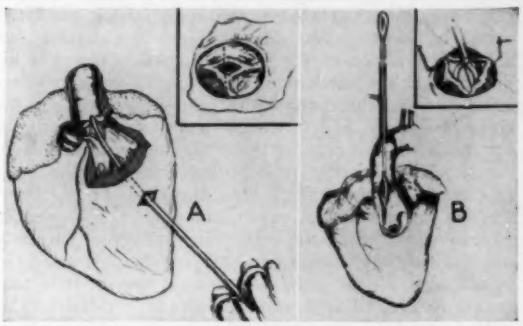

Fig. 6.—Left ventricular approach (*A*) to the aortic valve using instrument with retractable diamond-shaped cutting blades. The insert depicts fusion of valve cusps in aortic stenosis and the line of incision. Cervical approach (*B*) to the aortic valve through the right common carotid artery, innominate artery and ascending aorta. The insert shows the effect of the dilating instrument.

stenosis. Eventually even the slightest exertion produces dizziness and fainting. Persistence in exertional effort leads to greater discrepancy between supply and demand, both systemically and with regard to coronary flow. In all probability this may explain the frequency of sudden death after relatively moderate effort in patients with this type of lesion.

Experimental Considerations: The approach to the problems of stenotic valvular disease in the experimental laboratory is fraught with many difficulties. The experimental animal does not have valvular stenosis, nor can a reasonable facsimile of the human pathological picture be produced by methods yet devised. Therefore animal experimentation cannot follow the usual, accepted form but resolves itself into methods of surgical technic designed either to approach the valve itself or to by-pass it by involved methods of vascular anastomosis. Study of human heart specimens obtained at autopsy is likewise unsatisfactory because they usually represent extreme states of disease—a distortion of the conditions which may exist at the time when surgical intervention could reasonably be contemplated. Further, because fixation of the tissues has destroyed certain

important functional components such as mobility, bizarre conclusions are drawn.

The possible surgical approaches to the problem of aortic stenosis seem to take one of the following four courses: (1) replacement of the damaged valve by a section of transplanted aorta containing normal valves; (2) by-passing of the diseased valve by aortic transplants containing normal valves; (3) insertion of a mechanical valve, or (4) direct surgical attack on the stenotic valve itself. The possibilities of each of the first three (indirect) methods have been extensively explored experimentally in our laboratory and by others.[28] Although phases of this work are still under consideration, preliminary reports have been presented elsewhere [8c] and will not be repeated in this publication. It is sufficient to state that only occasional and unpredictable success has been attained by these experimental efforts and that the results do not warrant clinical trial at this early date. Operative hemorrhage, the maintenance of unobstructed coronary flow, the viability of tissue and valves so transplanted and many other problems have yet to be satisfactorily solved.

Direct Valvular Approach: It would seem reasonable that application of the methods successful in clinical mitral and pulmonary valve surgery might offer a ready solution. Certain inherent difficulties immediately arise, however, posed primarily by the nature and anatomic position of the stenosed aortic valve. It lies deep within the substance of the greatly hypertrophied left ventricle; the coronary ostiums and vessels are in close proximity, and no ready-made avenue for digital approach such as the auricular appendage is available. Incision through the myocardium close to the valve in the outflow tract of the left ventricle for the introduction of the finger or instruments is followed by excessive and uncontrollable hemorrhage. Similarly, approach through the aortic wall just distal to the valve is attended by the same danger. However, it is altogether feasible to approach the valve at greater distance both from the ventricular and from the aortic poles, as shown experimentally by Smithy and both experimentally and clinically by us.

Since the pulmonary and aortic valves are similar in construction and in method of action, the thought of performing a Brock type of operation for aortic stenosis seemed attractive. Therefore on March 9, 1950 at the Episcopal Hospital F.B., a white woman aged 26 with extreme aortic stenosis, was subjected to surgical operation. With a specially devised instrument equipped with retractable diamond-shaped cutting blades, entry into the left ventricle was made near its apex (a low pressure area as compared to the outflow tract) and the instrument guided into the stenotic valve orifice (fig. 6*A*). The retractable blades were opened, and the valve was cut vertically by pulling the instrument back into the ventricle. Although the wound was rapidly sutured, almost immediately the heart rate slowed and soon contractions ceased despite stimulation, rapid blood transfusion and prolonged cardiac massage. Autopsy revealed that the knife had been well placed and that despite the diffuse calcareous nature of the valve it had been divided into two halves. It was evident, however, that appreciable regurgitation had been produced, a condition incompatible with life when suddenly superimposed on diseased tissues. Attempts to apply the technics that were successful for the pulmonary and mitral valves had failed initially, and there was no reason to suppose that persistent application of the same principles would meet with a better fate. There remained the possibility of modifying the method of Tuffier,[12] who in 1914 successfully dilated the aortic valve of a young man with severe and progressive aortic stenosis. By invaginating the wall of the aorta just above the valve and pushing it into the stenosis on the forefinger, he was apparently able to accomplish dilatation of the valve sufficient to bring about reversal of the progressive course of this patient's disease, for as late as 1924 the patient was reported living and improved. On reexamination of our specimens of aortic stenosis with the possibility of dilatation in mind, it was again noted that the free edge of the cusps of the valve appears to bear the brunt of the disease process. The edge is thickened, indurated and tough, often calcified. By simple forceful dilatation in the laboratory it was possible to tear open one or more of the sealed commissures without injury to the valve cusp itself. Such an opening should produce little if any additional regurgitation, since the cusp as a whole will function better after mobilization. True, it would be unusual for all three commissures to tear open with restoration of essentially normal valve function. However, the powerful hypertrophied left ventricle, able as it is to compensate until veritably only a trickle of blood can pass the aortic barrier, will readily respond to even moderate relief of the obstruction.

We therefore devised an instrument that is shaped like a large pencil with a blunt point. This is inserted through an incision in the neck into the lumen of the right common carotid artery. It is gently guided through the innominate artery into the ascending aorta and soon impinges on the aortic valve. The valve is readily recognized both by resistance to further passage and by the direct transmission of the cardiac movements to the operator's hand through the instrument. The valve orifice can readily be located, the instrument engaged within the narrowed lumen and inserted well into the ventricle (fig. 6*B*). The dilating mechanism near the tip is then gently opened by a turnscrew on the handle of the instrument, gradually dilating the cusps to or past the point of commissural separation. Blood flow through the aortic orifice is maintained by a lack of continuity of the dilating surface. The instrument is then closed and removed; the carotid incision is repaired by a continuous suture of arterial silk.

This operation has been performed recently on two patients with multivalvular lesions, one of which was severe aortic stenosis. Both patients, although far advanced in the course of their disease and in relatively poor condition, withstood the procedure well. Postoperatively both presented objective evidence of enlargement of the aortic valve orifice, and both appear clinically improved. Because of associated myocardial disease and coexistent mitral regurgitation, neither was considered suitable for major thoracotomy and direct attack on the heart. Both patients underwent operation recently and have not reached a point at which significant conclusions can be drawn regarding the eventual effect of their valvular dilatation.

SUMMARY AND CONCLUSION

Our entire experience with the surgical management of stenotic valvular disease has been reviewed. The fact that pulmonary valvular and infundibular stenosis can be relieved by the direct surgical approach as devised by Brock and modified herein has been confirmed. Initial results with the direct ventricular approach are at least comparable with those of earlier shunt procedures, and the prospect that the patient will have more nearly permanent relief and a more certain future after the

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direct approach seem to outweigh present doubt as to the eventual physical havoc that may result from the surgically produced shunts of earlier technics.

Commissurotomy accomplishes relief of mitral stenosis by restoring a considerable degree of valve function without the production of significant mitral regurgitation. That this type of surgical intervention can be performed with a reasonably low mortality has been demonstrated. There has been no return of the stenotic state detectable clinically or physiologically in two early cases followed for a period of two and one-half years or in any more recent cases.

In aortic stenosis dilatation of the aortic valve would appear to be the surgical treatment of choice at the present time. Whether this surgical objective is best achieved from the aortic or ventricular approach is conjectural. Considerable time must elapse for evaluation of present methods.

ADDENDUM

Since this paper was submitted for publication many additional patients have been treated surgically. The total cases to date (October, 1950) include: pulmonary stenosis in tetralogy of Fallot (consecutive), 15 (six infundibular and nine valvular) with two deaths (one infundibular and one valvular); mitral stenosis, 86 (60 so far in 1950) with four deaths, mortality 6.6 per cent, and aortic stenosis, five with two deaths.

230 North Broad Street (2).

CONVERSION OF THE AURICULAR APPENDAGE INTO A LEAKPROOF VALVE TUBE FOR INTRACARDIAC SURGERY

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One of the most important steps in successful intracardiac surgery is the prevention of hemorrhage from the heart. Control or prevention of cardiac hemorrhage can be accomplished in a number of ways. The simplest and most frequently used method is a purse-string suture, or opposing purse-string sutures around the wound of entrance.

I am presenting a method for the control or prevention of cardiac hemorrhage during intracardiac surgery by the creation of a valve tube, using the auricular appendage. To my knowledge this method has not been previously described. It was perfected in the surgical research laboratory on dogs and has been used on two human beings.

The auricular appendage lends itself admirably to the creation of a valve tube because its walls are thin and pliable and it can be easily elevated or invaginated into the cavity of the auricle. The appendage hangs down on the outside of the auricle like a dog's ear and is actually a small secondary extra-auricular chamber of the heart. The opening of the appendage into the auricle is large, and when the tip end of the appendage is held away from the side of the auricle it forms an irregular flattened triangular or cone-shaped pocket.

Conversion of this cone-shaped pocket into a valve tube which is leakproof and which can be used without haste and repeatedly at any one operation for intracardiac digital or visual examination or for surgical intervention is accomplished by placing two sets of opposing purse-string sutures.

After the pericardium is opened, the tip of the appendage is picked up and held steady by a noncrushing clamp. A site is now selected on the appendage, just proximal to the tip, which is judged to be of sufficient diameter to admit the instrument or palpating finger. At this site opposing purse-string sutures are placed. The suture material which I prefer is number 0000 black silk on an atraumatic needle. The first suture is on the upper or outer surface of the appendage and consists of three bites. The first needle bite is near the edge of the appendage on its upper surface, the second needle bite is in the center of the upper surface and the third bite is near the opposite edge of the upper surface as is shown in figure 1 *A*. The second purse-string suture is placed in a similar manner on the under or cardiac surface of the appendage at a point directly opposite the first suture. Since the purpose of these sutures is to form a valve which can be repeatedly opened and closed, their proper placement is important. The first set of purse-string sutures forms the outer valve.

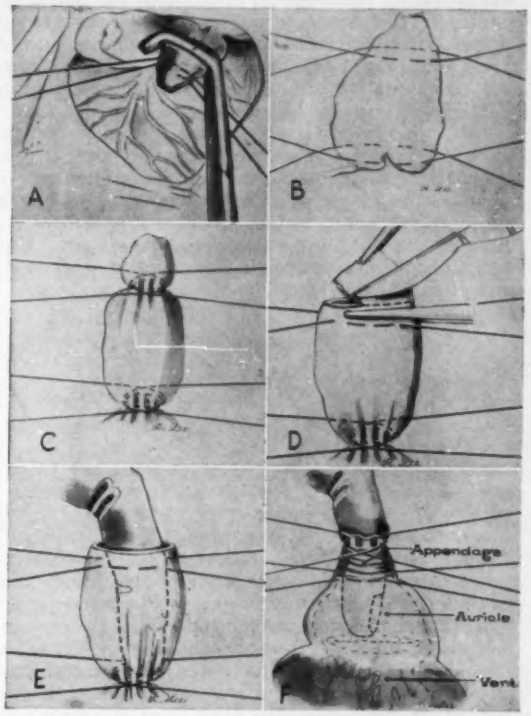

Fig. 1.—*A*, opposing anterior and posterior purse-string sutures are placed near the tip of the appendage. The sutures go through the entire thickness of the wall of the appendage and form the outer valve. *B*, a second row of anterior and posterior opposing purse-string sutures is placed near the base of the appendage to form the inner valve. The appendage is elevated to show the tubelike effect. *C*, creation of the valves is accomplished by a purse-string pull on the opposing sutures. When the sutures are relaxed the appendage returns to its normal shape. *D*, the inner valve is closed to prevent a leakage from the auricle, and the tip of the appendage is cut off. *E*, a finger or instrument is now inserted through the relaxed outer valve down to the closed inner valve of the appendage. *F*, when the tip of the finger has reached the closed inner valve, the outer valve is now closed, the inner valve relaxed and the finger or instrument is inserted into the auricular cavity by invagination of the appendage. Removal of the finger or instrument is accomplished by reversing the procedure.

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The second set of opposing purse-string sutures is now placed at the base of the appendage just distal to the auricle. The first suture consisting of three needle bites is placed in a manner parallel to the first suture of the first set, and the second suture is parallel to the second suture of the first set. This second set of sutures forms the inner valve (fig. 1 *B*).

The sutures go through the entire thickness of the wall of the appendage and when pulled in the manner of purse strings will completely approximate the walls at that point and thus act as a valve and close any existing opening (fig. 1 *C*). However, when the sutures are pulled in the opposite direction of a purse string, they pull the walls of the appendage away from each other and tend to relax and hold open any existing opening. Thus the valves may be closed or relaxed at will by merely reversing the direction of the pull on the sutures. These opposing purse string sutures are not tied until the intracardiac surgical procedure is finished. The use of curved and straight clamps and of different size clamps on the suture ends helps the operator to identify each suture at a glance.

When the inner valve is closed by pulling on the second set of sutures in a purse-string manner, this completely occludes the auriculoappendical opening and separates the auricle from the appendage. As long as the inner valve is closed any manipulation or opening distal to this point causes no loss of blood other than the small amount contained in the appendage itself at the time of the valve closure.

Fig. 2.—At the conclusion of the operation the proximal purse-string sutures are tied securely and the part of the appendage distal to this ligature is amputated.

After the two sets of sutures are placed, thus forming an outer and an inner valve and converting the appendage into a tube, the inner valve is closed and held closed by proper suture pull. The tip end of the appendage just distal to the outer valve is now completely cut off by scissor or scalpel, and this opening is relaxed by proper suture pull on the outer valve (fig. 1 *D*). The palpating finger or instrument is inserted through this opening down to the inner valve (fig. 1 *E*). The first set of sutures forming the outer valve is now pulled in a purse-string manner and the outer valve is closed and held closed around the finger or instrument. The inner valve is now released by reversing the suture pull to allow the finger or instrument to enter the auricle and proceed, if desired, through the auriculoventricular valve into the ventricle (fig. 1 *F*). The appendical musculature is thin and pliable and lends itself easily to invagination.

At the end of the maneuver the finger or instrument is withdrawn just distal to the inner valve and this valve is again closed off by proper suture pull. When the inner valve is closed the outer valve is relaxed and the finger or instrument is withdrawn entirely from the appendage. The entrance and exit may be repeated a number of times. When the operation is finished, the sutures forming the inner valve are pulled tight and tied securely, and that portion of the appendage distal to the sutures is cut off completely (fig. 2). Amputation of the appendage after purse-string suture is followed by excellent healing without mural thrombosis.[1]

CONCLUSION

The creation of an outer and inner valve which can be closed or relaxed at will gives the surgeon the opportunity for digital or instrumental examination before and after intracardiac surgery without fear of hemorrhage and without undue haste. The auricular appendage is well suited for the creation of such a valve tube. It is important that the sutures be placed at a definite site and in a definite manner. It is also important that the opening in the distal end of the appendage be large enough to easily admit the palpating finger or an instrument, without stretching or tearing the mouth of the opening.

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CORTICAL STEROIDS IN TREATMENT OF CANCER

Observations on Effects of Pituitary Adrenocorticotropic Hormone (ACTH) and Cortisone in Far Advanced Cases

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and
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It is now well established that androgenic and estrogenic steroids produce temporary regression of malignant tissue of the breast [1] in certain cases and that estrogenic steroids also have an anticarcinogenic effect on prostatic cancer.[2] There is also some evidence that progesterone may have a similar effect on carcinoma of the cervix,[3] breast [4] and prostate.[5] When pituitary adrenocorticotropic hormone (ACTH) and cortisone became available for clinical trial, it seemed logical to attempt to evaluate their effect on various types of malignant lesions. Murphy and Sturm [6] reported favorable results on transplanted leukemia in rats with

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From the Rush Department of Medicine and Pathology of the Presbyterian Hospital of the City of Chicago and the University of Illinois.

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Associate clinical professor of medicine (Rush), University of Illinois, and associate attending physician, Presbyterian Hospital (Dr. Taylor); resident in pathology, Presbyterian Hospital, and assistant in pathology, University of Illinois (Dr. Ayer), and research fellow, American Cancer Society, and clinical assistant in medicine (Rush), University of Illinois (Dr. Morris).

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pituitary adrenocorticotropic hormone or adrenal cortical extract. Heilman and Kendall [7] produced an arrest of the growth of malignant lymphoid tumor in the mouse with the administration of cortisone. Pearson and others [8] have reported temporary remission in Hodgkin's disease, acute leukemia and chronic lymphatic leukemia in man after use of the two drugs. We have previously reported [9] symptomatic improvement in cancer of the trachea, endothelial myeloma (Ewing's tumor) and carcinoma of the breast during pituitary adrenocorticotropic therapy. However, augmentation of breast carcinoma seemed to occur in one patient. Serious psychic changes occurred in three patients during prolonged therapy.

CLINICAL MATERIAL

The effect of pituitary adrenocorticotropic hormone and cortisone was studied on 26 patients with far advanced malignant disease. All but two of the patients had previously had surgical treatment and/or irradiation. Some patients in the lymphoma group had had extensive nitrogen mustard therapy before starting treatment with pituitary adrenocorticotropic hormone or cortisone. Although the clinical results on the disease process have been favorable in only a few patients, the physiological alteration produced by large doses of these drugs over a relatively long period of time have been of interest and may serve as a timely warning with the increasing availabiilty of these drugs. The following types of neoplasms were treated: 5 carcinomas of the breast, 1 carcinoma of the trachea, 1 carcinoma of the colon, 1 hypernephroma, 1 angioendothelioma (Ewing's sarcoma), 1 neurofibrosarcoma, 1 melanoma, 6 lymphosarcomas, 1 subacute myelogenous leukemia, 1 chronic lymphatic leukemia, 1 acute leukemia, 1 multiple myeloma, 3 Hodgkin's disease and 2 mycosis fungoides.

PROCEDURE

Metabolic balance studies were done on the first few patients, but as it became apparent that no new information was being obtained and that dangerous complications could be predicted adequately by clinical observations and less cumbersome laboratory technics, this was abandoned.

Serum sodium, potassium and proteins, sedimentation rate, hemograms and total eosinophil counts were done. Aliquots were saved for further study where indicated. Results of the Thorn test, 17-ketosteroid excretion and glucose tolerance test were determined for most patients before therapy. These tests were repeated during and after treatment. When feasible, pretreatment and post-treatment biopsies were obtained. Liver function tests and bone marrow aspirations were compared before, during and after therapy in certain patients. Daily weight and fluid balance were obtained.

Pituitary adrenocorticotropic hormone was given every six hours in doses of 25 to 50 mg. and cortisone in doses of 100 to 600 mg. daily in one or more doses. One patient inadvertently received a single injection of 175 mg. of pituitary adrenocorticotropic hormone. This produced vasopressin (pitressin®)-like effects but no untoward reaction. All patients were placed on a low sodium diet and given 3 to 4 Gm. of potassium chloride daily during treatment with the agents.

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RESULTS

The clinical response of most patients was reduction in fever, if present, increased appetite and improved strength and well-being. At times the effects were dramatic and appeared usually within 48 hours after starting pituitary adrenocorticotropic therapy and within four to six days after starting treatment with cortisone. This improved state lasted until side effects from long continued therapy ensued or complications produced by the progress of the neoplastic disease developed. Patients hitherto bedridden, vomiting and requiring heavy doses of narcotics were able to become ambulatory, reduce or stop their reliance on narcotics and eat astonishing meals within 48 hours after starting to take the former drug, or a few days later after starting to take the latter. Progressive anemia frequently was controlled, and in several patients the red blood cell count and hemoglobin level rose slightly. Results of liver function tests, if abnormal before treatment, improved. Elevated sedimentation rates were reduced, and jaundice disappeared.

These clinical signs of improvement were temporary, and relapse of the patient occurring shortly after omission of therapy was the rule. However, three patients with lymphosarcoma, one with Hodgkin's disease and one with chronic lymphatic leukemia have maintained this improvement as long as three months after omission of therapy. We have frequently been faced with the problem whether complications produced by continued therapy or relapse from omission caused more distress to the patient.

EFFECT ON TUMOR GROWTH

In no patient with carcinoma was there evidence of reduction in the size of the tumor with pituitary adrenocorticotropic hormone, although induration and edema around the site of the tumor frequently regressed. In three of the four patients with carcinoma of the breast, treated with this drug, the growth appeared to be augmented, although a carcinomatous ulcer healed in one.

Biopsies were obtained before therapy on four patients with cancer of the breast, and biopsies or autopsies were done immediately following therapy. Before this drug was given these patients had all had therapy: in three it consisted of radiation followed by sex steroids. One patient also had nitrogen mustard therapy, and one had had diethylstilbestrol therapy only. Because of these factors, interpretation of the anatomic effects of the drugs is impossible. No effect on the neoplastic growth could be demonstrated. The cells of the tumor were viable and actively proliferating. Metastases were widespread, occurring in the spleen, pancreas and gastrointestinal tract, bladder and lymph nodes. The spleens of two of the three patients with autopsy showed extraordinary extensive permeation by neoplastic cells (fig. 1), suggesting a decreased resistance of this organ to the neoplastic cell.

One patient (case 2) with carcinoma of the breast who was given cortisone showed reduction in the size of skin lesions with healing of ulceration. Biopsies, however, did not show changes in the malignant cells. Four weeks after omission of cortisone therapy, the lesions again ulcerated and new lesions appeared.

Repeated biopsies taken before, during and after therapy in the patient with carcinoma of the trachea (case 7) showed no cytological change in the tumor, and supraclavicular metastases appeared during therapy along with extension of the tumor above and below the initial site. However, carcinomatous ulceration

healed and edema subsided, producing an improved airway. No biopsy was obtained of the liver after therapy in the patient (case 6) with hepatic metastases from carcinoma of the colon, and no appreciable decrease in the size of the liver was observed.

of necrotic areas. These changes had already begun at the time of the first biopsy and were probably due to previous nitrogen mustard therapy. However, two subsequent biopsies showed further decrease in mitosis and increased fibrosis. The biopsy material on the

Results with Pituitary Adrenocorticotropic Hormone (ACTH) and

Case	Sex	Age	Disease State	Therapy: Drug	Therapy: Gm.	Duration of Course of Therapy (Days)	Change in Tumor During Therapy	Clinical Changes During Therapy	Present Status
1	F	59	Adenocarcinoma of breast, visceral metastases	ACTH	1.24	25	None	Edema, congestive failure and euphoria	Died 10 days after omission of therapy; autopsy
2	F	54	Adenocarcinoma of breast, local and axillary recurrences	Cor.	3.8	23	Reduction in size of skin nodules, no cytological change (serial biopsies)	Euphoria	Living 57 days after stopping therapy; lesions progressing
3	F	41	Adenocarcinoma of breast, visceral metastases	ACTH	3.85	24	Possible augmentation	Schizoid reaction; edema, moon face and hyponatremia	Died 6 days after omission of therapy; high fever; at autopsy, unusual invasion of spleen by neoplasm
4	F	33	Scirrhous carcinoma of breast: R., adenocarcinoma; L., visceral metastases	ACTH	2.25	23	Healing carcinomatous ulcer; augmentation of other lesions	Schizoid reaction following euphoria; control of vomiting, fever and pain; improved nutrition; became ambulatory	Died 2 days after omission of therapy; high fever; at autopsy, invasion of spleen as in case 3
5	F	73	Carcinoma simplex of breast, regional metastases	ACTH	1.15	19	Augmentation; no cytological change (serial biopsies)	Edema, congestive failure, moon face and mental confusion	Living 231 days after omission of therapy; mentally normal; lesion stationary
6	M	38	Carcinoma of colon, hepatic metastases	ACTH	2.98	35	None	Reduced fever; improved liver function and appetite; less pain; euphoria	Living 45 days after omission of therapy; nitrogen mustard administered into hepatic artery on omission of ACTH with reduced size of liver; liver function remains improved
7	M	63	Carcinoma of trachea	ACTH Cor. ACTH ACTH ACTH	8.8 3.0 1.6 1.2 0.6	90 15 20 15 12	Healing carcinomatous ulcer; no cytological change (serial biopsies)	Relief of bronchial spasm; most signs of Cushing's syndrome; hypomania, pneumonia on omission; pigmentation	Living; still receiving repeated courses of ACTH; tumor progressing
8	M	22	Hypernephroma; skeletal and visceral metastases	ACTH	1.5	15	None (serial biopsies)	Moon face, edema and acne	Living; progression of disease
9	M	15	Angioendothelioma with metastases	ACTH	4.187	34	Progressively decreasing mitoses and fibrosis (serial biopsies)	Control of fever, vomiting and anemia; most signs of Cushing's syndrome; mental confusion	Died 4 mo. after omission of therapy; no autopsy
10	M	23	Neurofibrosarcoma; pulmonary axillary metastases	ACTH	1.67	20	None	Euphoria; decreased pain; improved movement of affected joint; less induration	Living 30 days after omission of therapy; pain recurring; induration the same
11	M	52	Melanoma, visceral metastases	ACTH	1.7	17	Hemorrhage into abdominal metastases; melanotic infiltration of skin; serial biopsies; no change	Reduction of fever, decreased pain, increased appetite; edema, euphoria and restlessness	Died 49 days after omission of ACTH; at autopsy, no change in the tumor, further progression of disease
12	M	54	Lymphosarcoma	ACTH	2.225	26	Decrease in size of cervical nodes; serial biopsies; no change	Relief of abdominal pain, improved appetite; euphoria, edema and pigmentation	Died 14 days after omission of ACTH; no autopsy; fever, rapid growth of nodes, anemia
13	F	44	Lymphosarcoma	ACTH ACTH	2.235 2.7	26 29	Decrease in size of involved nodes and abdominal masses, 1st course; serial biopsies, no reduction, 2d course	Relief of pain, improved appetite; edema, pigmentation and euphoria	Living on therapy; relapse immediately after therapy, despite nitrogen mustard and radiation; 2d course did not produce clinical improvement
14	F	49	Lymphosarcoma	Cor. ACTH Cor.	3.0 1.995 4.0	24 14 29	Decrease in size of nodes with cortisone; no change with ACTH; serial biopsies, no change	Decreased abdominal pain, fever and nausea controlled with cortisone; relapse on changing to ACTH; second course of cortisone, no improvement	Died 3 wk. after last course of cortisone
15	F	67	Lymphosarcoma	Cor. Cor. ACTH	3.79 0.710 1.96	27 9 15	Decrease in size of nodes with cortisone; no effect with ACTH; serial biopsies, decreased mitosis	Marked increase in strength; improvement lasted 6 weeks, after cortisone was omitted; no improvement with ACTH	Discharged from hospital in terminal condition; died 2 wk. later; no autopsy

Biopsies before and after pituitary adrenocorticotropic therapy on metastatic lesions in the patient (case 8) with hypernephroma revealed no change, and there was no visible evidence of tumor regression. Biopsies of the endothelial myeloma before and after therapy showed the development of areas of necrosis, slightly decreased mitotic activity and proliferative fibrosis at the margins

neurofibrosarcoma was unsatisfactory, but no evidence of regression of the tumor was noted clinically.

The one case of melanosarcoma treated with the adrenocorticotropic agent at autopsy displayed widespread, wildly growing metastases. The patient with subacute myeloid leukemia showed no change in the peripheral blood or bone marrow following pituitary

adrenocorticotropic therapy. This was also true of a child with acute leukemia. Although there was a decided reduction in the size of the spleen, liver and lymph nodes in the patient with chronic lymphatic leukemia, no changes were noted in the biopsies of the nodes or in the bone marrow aspiration studies. After 14 days of pituitary adrenocorticotropic therapy, the bone marrow studies of the patient with multiple myeloma had shown no change in the percentage of myeloma cells.

All three patients with Hodgkin's disease showed major regression in the size of the tumor. One patient (case 18) has been suitable for repeated biopsies. This patient had previously had what was considered maximal radiation and nitrogen mustard therapy. Radiation had been given one month before the biopsy specimen was taken prior to pituitary adrenocorticotropic and cortisone therapy. This showed areas of necrosis, fibrosis, vascular proliferation and endarteritis obliterans, changes which are usually associated with the effects of roentgen and nitrogen mustard therapy. These areas showed little tendency to increase in size with hormonal or cortisone therapy. A profuse eosinophilia was seen in a biopsy from a lymph node over a month after institution of therapy with pituitary adrenocorticotropic hormone.

One patient (case 15) with lymphosarcoma (figs. 2 and 3) had received roentgen therapy to tolerance before treatment with the two steroids. Another (case 14) had not received prior treatment. Both

Cortisone Therapy on Patients with Advanced Neoplastic Disease

Case	Sex	Age	Disease State	Therapy: Drug	Therapy: Gm.	Duration of Course of Therapy (Days)	Change in Tumor During Therapy	Clinical Changes During Therapy	Present Status
14	M	29	Lymphosarcoma	ACTH ACTH	2.125 2.550	28 31	Decrease in size of liver and spleen	Fever reduced, cough controlled, chest cleared, appetite improved; blood count improved; jaundice cleared; relapsed 2 wk. after 1st course of ACTH; second remission with 2d course; acne, Cushing's facies	Living; returned to work after disability of 1 yr.; liver and spleen not palpable; good health 3 mo. after 2d course of therapy
17	F	63	Lymphosarcoma of liver and spleen with ascites	ACTH	1.810	26	Liver biopsy at onset of therapy, not repeated; liver and spleen greatly reduced in size	Sulfobromophthalein excretion improved; increased vigor; edema, euphoria	Living; improvement maintained 35 days after omission of therapy
18	F	37	Advanced Hodgkin's disease (onset 3½ yr. prev.)	ACTH ACTH Cor. Cor. ACTH	1.408 0.300 4.8 6.7 1.04	18 3 25 41 14	Decrease in size of nodes during therapy with recurrences within 1-2 wk. after omission (serial biopsies)	Jaundice, itching and fever controlled; severe signs of Cushing's syndrome	Living 217 days after therapy instituted; disease in remission for 1-2 wk. after therapy omitted; several times has appeared terminal but improved with course of therapy; in remission 1 wk. after omission of therapy
19	M	28	Hodgkin's disease of liver (duration 3 mo.)	ACTH	1.705	20	Nodes reduced; liver and spleen decreased in size	Jaundice disappeared; alk. phos. from 38.1 to 12 U.; bilirubin from 7.17 to 1.21 mg.; sulfobromophthalein from 44.5 to 9.77% retention; vomiting controlled; size of liver, spleen and nodes decreased; acne, pronounced euphoria	Continues in remission 107 days after omission of ACTH
20	F	24	Hodgkin's disease (duration 3 mo.)	ACTH	2.910	37	Pelvic mass decreased in size	Fever and pain controlled; immediate relapse on omission of therapy	Given nitrogen mustard for relapse after ACTH; in remission 2 mo. after nitrogen mustard
21	F	34	Chronic lymphatic leukemia (duration 1 yr.)	ACTH	1.705	18	Spleen, liver and nodes decreased; serial biopsy, no change; hemogram unchanged	Increased comfort due to reduction in size of spleen; belligerency developed; WBC rose from 24,000 to 40,000	Hemogram and splenomegaly continued improved 90 days after omission of drug; gradual decrease in lymphocytes and total WBC
22	M	45	Subacute myelogenous leukemia (duration 2 yr.)	ACTH	2	20	Progressive leukopenia	Increased bleeding tendencies; gradual deterioration; development of abscesses; pigmentation	Died 42 days after omission of therapy
23	F	3	Acute myelogenous leukemia	ACTH	0.6	11	No change in hemogram	Progressive downhill course; glycosuria developed 9th day of therapy	Died 6 days after omission of drug
24	F	56	Mycosis fungoides (duration 25 yr.)	Cor. ACTH Cor. ACTH	1.573 0.675 1.3 2.98	10 7 8 36	Few lesions healed; most progressed	Slight euphoria and severe edema; congestive failure; serum Na dropped to 119, K rose to 6.1 mEq. with decreased Na and increased K excretion; fulminating infection after omission of ACTH; glycosuria	Died with pneumonia 66 days after institution of first course of cortisone
25	F	55	Mycosis fungoides (duration 15 yr.)	ACTH ACTH ACTH ACTH	3.972 2.575 1.725 3.290	50 30 20 37	Healing of 80% of lesions; no new lesions appeared during therapy; less malignant-looking cells on serial biopsies; relapse with new lesions on omission of drug	Psychosis developed; diabetic acidosis, hypokalemia with ECG changes; Cushing's facies; immediate control of pruritus and fever. Relapse on omission of the drug	Died of pneumonia on omission of ACTH, 254 days after institution of therapy
26	M	58	Multiple myeloma	ACTH	1.5	15	Bone marrow showed no change	Restlessness, increased previous depression; muscular weakness	Unchanged, still receiving ACTH

biopsies obtained before therapy were similar and had characteristics typical of the disease. Treatment with cortisone resulted in the following changes:

There occurred partial but well defined reduction in the size of the tumor, liver and spleen. There were areas of necrosis with surrounding zones of pale, edematous, proliferating fibrous tissue which increased as therapy was continued or repeated. Between the areas of necrosis and fibrosis large islands of actively proliferating neoplastic reticulum cells occurred. These cells were similar to those seen before cortisone therapy, except that the number of mitotic figures appeared to be slightly decreased and the fragility of the cells appeared to be increased with resultant filamentous forms in large numbers. Subsequent pituitary adrenocorticotropic therapy resulted in progression of the changes and occurrence of an unusual edematous mucoid alteration of the collagen.

Measurement of changes in the tumor of the other three cases of lymphosarcoma were based on reduction in the size of the spleen, liver and abdominal masses,

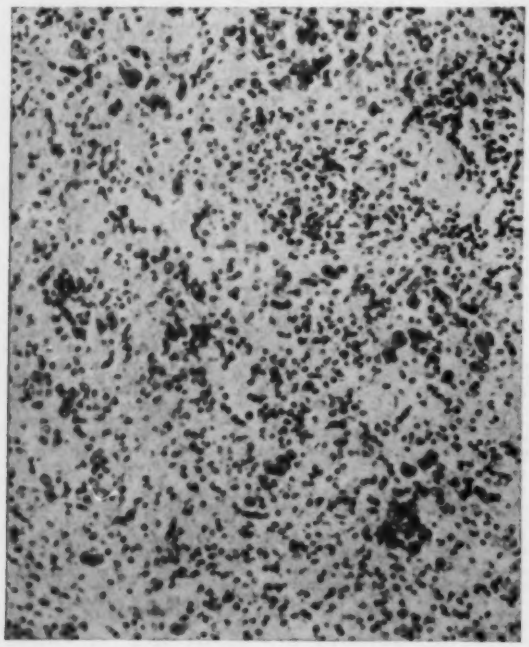

Fig. 1 (case 4).—Spleen demonstrating diffuse permeation of the pulp with metastatic tumor following therapy with pituitary adrenocorticotropic hormone.

which occurred in all to a pronounced degree. These changes have been maintained for 3 months in one and 1 month in another. The abdominal mass, previously proved to be tumor by biopsy, rapidly increased in size two weeks after treatment with the drug was omitted and has not regressed during a second course of therapy.

Grossly, the lesions of the two patients with mycosis fungoides responded differently to adrenocorticotropic therapy. While one showed pronounced regression and healing of about 90 per cent of the lesions with no new lesions appearing during therapy, the other showed healing of only 10 per cent of the lesions. Cortisone appeared to be of more value to the patient who responded poorly to pituitary adrenocorticotropic hormone:

Histologically both patients had lesions consistent with mycosis fungoides before treatment. Both patients had received innumerable types of therapy previously, including radiation and antibiotics. Treatment with pituitary adrenocorticotropic hormone resulted in a decrease in acanthosis, a diminished amount and diminished acuteness of inflammatory reaction in the corium, a

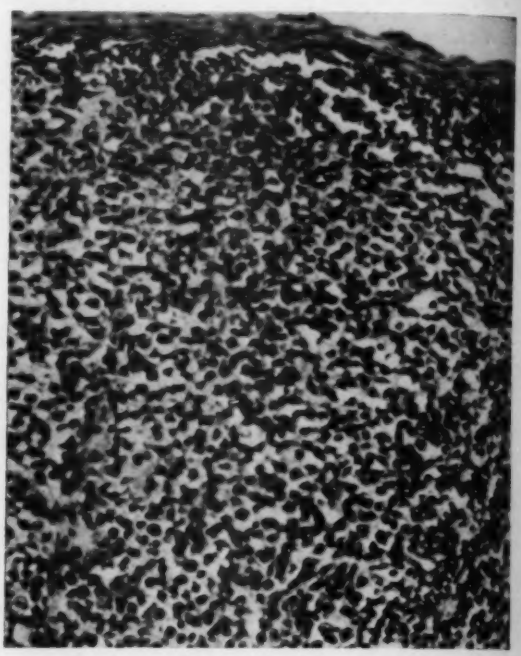

Fig. 2 (case 15).—Lymph node of lymphosarcoma before pituitary adrenocorticotropic hormone and cortisone therapy.

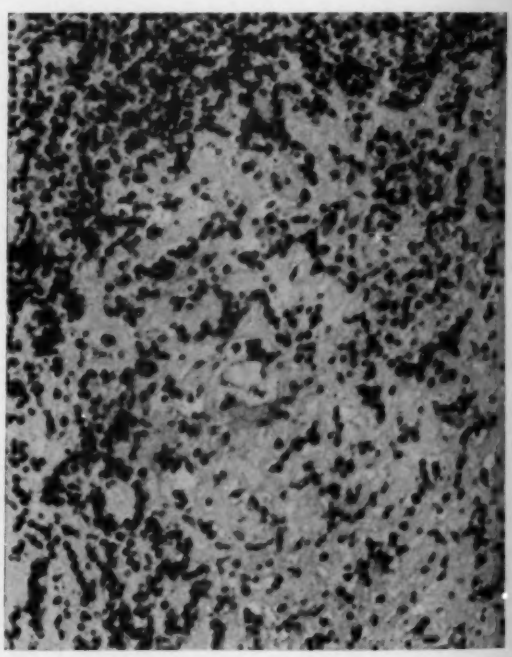

Fig. 3 (case 15).—Lymph node of lymphosarcoma showing progressive fibrosis and necrosis during therapy with the drugs.

slightly decreased number of immature reticuloendothelial cells with less mitotic activity and a diffuse proliferative fibrosis similar to that seen in the granulation tissue of healing wounds. The

inflammatory reaction diminished first in the deeper corium; the first cell to disappear was the eosinophil, followed by the polymorphonuclear leukocyte. Microabscesses of Pautrier in the epidermis also disappeared. The changes noted were of degree only, and the qualitative characteristics of the disease persisted. Correlation of the histological observations to the clinical course was not possible, the changes of the former usually being delayed. Periods without therapy resulted in a slight reversion of the condition to that before treatment. Reinstitution of therapy caused a mild improvement as judged by histological means.

It is difficult to draw conclusions because of the variability of the site of biopsy, the natural course of the disease and the effects of previous therapy. At autopsy both patients had severe pyogenic infections, and one had neoplastic masses in the lymph nodes, liver, lungs and peritoneum as well as the skin.

COMPLICATIONS FROM TREATMENT

The physiological alterations producing complications in our patients with extended pituitary adrenocorticotropic or cortisone therapy can be divided into: (*a*) electrolytic disturbances; (*b*) decreased glucose tolerance; (*c*) mental changes; (*d*) altered response to infection; (*e*) pigment disturbances; (*f*) sexual disturbances, and (*g*) Cushing's syndrome.

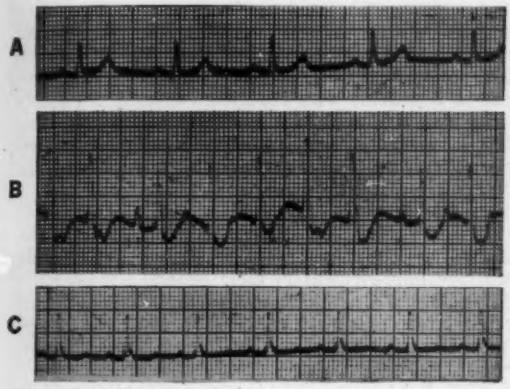

Fig. 4 (case 25).—Electrocardiographic changes in lead 2 during acute hypokalemia produced by prolonged pituitary adrenocorticotropic therapy. Note depression of the S-T segment with inversion of the T wave and progressive auriculoventricular block. *A*, Oct. 26, 1949 the heart rate was 64; the serum potassium level had been 4.1 milliequivalents per liter Sept. 21, 1949. *B*, Jan. 1, 1950 the heart rate was 140 and the serum potassium level 1.8 milliequivalents. *C*, Jan. 7, 1950 the heart rate was 100 and the serum potassium level 4.2 milliequivalents.

(*a*) *Electrolytic Disturbances.*—Disturbances Due to Sodium Retention: Edema occurred in 16 of 25 patients treated with pituitary adrenocorticotropic hormone and four of five treated with cortisone. This produced a serious problem in four patients requiring reduction or omission of the drug. Severe congestive failure was produced in three patients because of this. Hypernatremia did not occur in any patients, but hyponatremia of 112, 119 and 125 milliequivalents of sodium per 100 cc. of serum appeared in two patients despite decreased sodium retention. Hypertension did not occur in any patients.

Disturbances Due to Potassium Loss: Muscular weakness occurred in 19 cases. This may have been due to loss of potassium from the tissues. In two patients hyperkalemia developed despite pronounced potassium loss and evidence of tissue potassium deficiency. In only one patient did there develop acidosis and hypokalemia with typical electrocardiographic changes and the Wenckebach phenomenon (fig. 4). She also had decided glycosuria. Intravenously given potassium and control of the diabetes produced a return to normal electrocardiographic observations.

(*b*) *Decreased Glucose Tolerance.*—A change from normal glucose tolerance curve to a diabetic curve occurred in 11 of 14 patients given this test, both with pituitary adrenocorticotropic hormone and cortisone. Glycosuria and hyperglycemia that persisted for six weeks after the cessation of therapy occurred in a patient with a previously normal glucose tolerance. One patient manifested hypoglycemia after receiving the former drug. The blood sugar level fell to 34 mg. per 100 cc. of blood or less one hour after the patient received 100 Gm. of glucose orally or intravenously on three occasions.

(*c*) *Mental Changes.*—In all but four patients personality changes occurred. Euphoria was noted in 22. This has previously been described in patients treated for rheumatoid arthritis as the result of improved general conditions. Hypomania developed in three patients and frank schizoid reactions occurred in three others. Most patients complained of sleeplessness, restlessness and inability to concentrate. A few stated that their minds became too active. Depressed states frequently followed the above reactions. Two patients became suicidal. In no case, however, did the character change persist over three weeks after discontinuation of therapy.

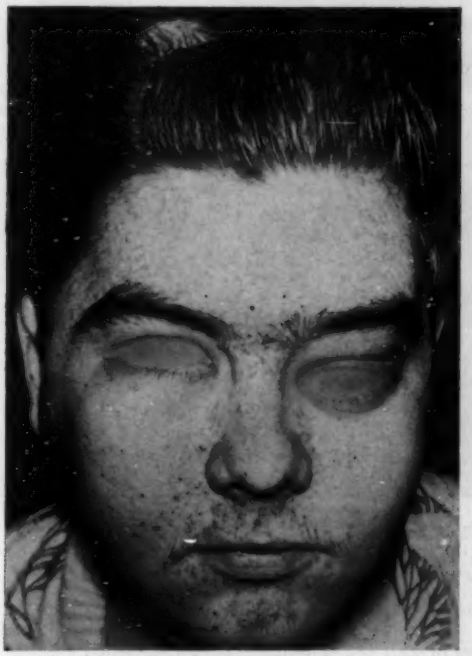

Fig. 5 (case 9).—Moon face and acne of Cushing's syndrome produced by pituitary adrenocorticotropic hormone, 100 to 150 mg. daily for three weeks (angioendothelioma).

(*d*) *Altered Response to Infection.*—When the dose of either of the two drugs was reduced or stopped, several patients had fever, at which time evidence of pneumonia or other respiratory infection was first noted. A reinstitution of full doses of the drug has produced control of fever but not necessarily a disappearance of the infection. This sudden onset of evidence of infection occurred less frequently when withdrawal of the drug was gradual. It is possible that when the drug is withdrawn abruptly a temporary hypoadrenocortical state is produced. Another possible explanation is that therapy masks the infection, preventing the usual febrile reaction until withdrawal of the drugs.

(*e*) *Pigment Disturbances.*—Eleven of the patients given pituitary adrenocorticotropic hormone or cortisone displayed greatly increased pigmentation of the skin and darkening of moles while they were receiving the drugs. Two patients had pigmentation in the buccal mucosa, as seen in Addison's disease. The patient with melanoma had melanotic infiltration, absent before treatment, in an abdominal scar.

(*f*) *Sexual Disturbances.*—Amenorrhea developed in the two patients previously having regular periods. Both patients experienced vasomotor disturbances. Acne occurred in eight patients during pituitary adrenocorticotropic therapy and in two during cortisone therapy (fig. 5). Hirsutism occurred in seven of the female patients and in one preadolescent boy.

(*g*) *Cushing's Syndrome.*—Cushing's syndrome with remarkable changes in the face, fat deposits on the shoulder and neck, abdominal protrusion, acne and hirsutism occurred in three patients who received continuous or frequently repeated courses of therapy for five weeks, three months and six months, respectively. This disappeared gradually over a period of six weeks without therapy, but became an exceedingly distressing complication in one previously good-looking woman (fig. 6).

ANATOMIC CHANGES PRODUCED BY PITUITARY ADRENOCORTICOTROPIC THERAPY

Autopsies on six patients who had received pituitary adrenocorticotropic hormone showed that there had occurred a moderate hyperplasia of the adrenals (average weight 10.9 Gm.), a decrease in the size of the thyroid gland (average weight 18 Gm.) and degenerative changes of the female genitalia. The pituitary gland contained variable numbers of eosinophils, basophils and chromophobe cells, and no conclusion could be drawn. Crooke cells were not noted. All the patients had extensive pyogenic infection involving the skin, lungs or kidneys. The patients had the usual number of fibrous adhesions of the serous membranes and benign tumors. The structure of the latter did not appear to be altered by the hormone. Biopsies and specimens obtained at autopsy showed an increased number of macrophages containing melanin. Normal skin and lymphatic tissue did not appear to be affected by the drug.

Fig. 6 (case 18).—Patient with advanced Hodgkin's disease (*A*) six months prior to cortisone therapy; *B*, Cushing's syndrome produced by 11.5 Gm. of cortisone given over a 90 day period. Note the fat pads on the shoulders and the moon face.

COMMENT

The nonspecific beneficial effect of pituitary adrenocorticotropic hormone and cortisone in patients not showing tumor regression is a phenomenon on which it is interesting to speculate. It may represent an inhibition of the local tissue reaction to the tumor, analogous to the inhibition of the tuberculin reaction produced in hyperimmune guinea pigs by cortisone, as reported by Stoerk.[10] Dramatic improvement in breathing occurred in a patient with carcinoma of the trachea; this has been repeatedly produced with decreased inflammatory reaction around the tumor and relief of bronchial spasm with courses of one or the other drug for the last 13 months, although the tumor itself has been progressing. Reduction in fever is characteristic in other diseases treated with the drugs.[11] This does not appear to be a typical antipyretic reaction, as it is not associated with sweating. This again may be related to inhibition of tissue reaction.

In only the patients with lymphosarcoma, chronic lymphatic leukemia and Hodgkin's disease does there appear to be any worth while benefit. However, most of these patients show improvement only when side effects become troublesome and at times alarming; they then relapse before complete recovery from these side effects has occurred, making further therapy impossible or unwise.

Only one patient with Hodgkin's disease has had a remission, lasting four months. This patient has Hodgkin's disease of the liver, the disease being of recent origin and previously untreated.

SUMMARY AND CONCLUSIONS

Twenty-six patients with advanced neoplastic disease have been treated with pituitary adrenocorticotropic hormone (ACTH) or cortisone. The former was given in doses of 100 to 200 mg. daily, for individual periods of two weeks to three and one-half months. The latter was given in doses of 100 to 300 mg. daily for similar periods.

Temporary regression of neoplastic lesions were produced in 3 patients with Hodgkin's disease, 5 patients with lymphosarcoma and 1 patient with chronic lymphatic leukemia. A doubtful regression of angioendothelioma (Ewing's sarcoma) occurred with pituitary adrenocorticotropic hormone.

Patients with carcinoma, acute leukemia, myelogenous leukemia and melanoma showed no control of the neoplastic disease, but most patients manifested striking temporary improvement in their general condition.

Physiological alterations produced by these hormones given in large doses make repeated or prolonged therapy ill advised.

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Cerebral Hemorrhage and Cerebral Embolus.—The diagnosis of cerebral embolus is indicated whenever there is a sudden onset of neurologic symptoms in a patient with an acute or chronic endocarditis, auricular fibrillation, a recent coronary thrombosis, septicemia or a septic focus. These cases often present clinical evidence of embolic phenomena elsewhere in the body. The differential diagnosis between cerebral hemorrhage and thrombosis is difficult since both occur in patients of the same age group and in patients with arteriosclerosis and hypertension. Several points in the history and physical examination make this differentiation possible in the majority of the cases: 1. Convulsions at the onset favor an intracerebral hemorrhage since they occur in about 14 per cent of such cases and in only about 7 per cent of the patients with a cerebral thrombosis. 2. The occurrence of severe headache, nausea or vomiting at the onset favors the diagnosis of cerebral hemorrhage. 3. Cheyne-Stokes or labored respirations are much more common in cases of cerebral hemorrhage. The same is true of conjugate deviation of the eyes. 4. Stiffness of the neck, quadriplegia and bilateral Babinski's toe sign occur in a much higher percentage of the cases of cerebral hemorrhage. 5. A bloody cerebrospinal fluid is diagnostic of a cerebral hemorrhage.—*Proceedings First National Conference on Cardiovascular Diseases,* American Heart Association and The National Heart Institute, U. S. Public Health Service, 1950.

HOMOLOGOUS SERUM JAUNDICE

Report of Eight Fatal Cases

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The occurrence of jaundice after the administration of human tissue products was first described by Hirsch,[1] who observed that jaundice developed in 14.8 per cent of 1,289 persons vaccinated for smallpox with "humanized lymph" in glycerin. A similar observation was made by Lürman[2] in 1885. By 1908 Weber[3] had collected from the literature 53 cases of acute yellow atrophy appearing in patients who had been treated in clinics for syphilis. Theiler[4] in 1918 observed jaundice in horses following the injection of homologous serum.

However, it was not until 1937 that the first report of the development of hepatitis after the injection of a preparation containing, among other substances, human blood serum appeared. In that year Findlay and MacCallum[5] reported the occurrence of hepatitis among British troops after yellow fever vaccination. Since this report hepatitis has been noted to result from the administration of convalescent measles serum[6] and mumps serum,[7] from immunization against sand fly fever[8] and from yellow fever vaccinations.[9]

The major impetus for the careful and detailed investigation of the cause of hepatitis following the introduction into the body of products containing human serum was provided by the report of 28,585 cases of hepatitis, with 62 deaths, occurring between Jan. 1 and July 4, 1942, among U. S. Army personnel who had been inoculated with yellow fever vaccine.[10] The extensive investigations of Sawyer and his co-workers[11] and earlier by Findlay and associates[12] definitely incriminated the human serum in the vaccine as the source of the icterogenic agent. The human serum component of the vaccine was eliminated after this outbreak.

The term homologous serum jaundice was first used in a memorandum prepared by medical officers of the British Ministry of Health in 1943.[6b] Hepatitis from both plasma and blood was mentioned at this time. Subsequent reports[13] would indicate that serum jaundice from whole blood was less common than from pooled plasma or serum. Spurling, Shone and Vaughn,[14] in a well controlled study, reported an incidence of 7.3 per cent of jaundice cases in 1,054 persons receiving serum or plasma but no definite cases in 891 others given a total of 2,278 transfusions of whole blood.

Bigger[15] in 1943 presented suggestive evidence that hepatitis may be spread by contaminated syringes. Outbreaks of jaundice have been reported in syphilitic,[16] diabetic[17] and arthritic clinics,[18] in a tuberculosis sanatorium[19] where monthly blood samples for sedimentation rates were taken, and after injections of penicillin[20] and acriflavine.[21] Cases of serum jaundice after thiopental (pentothal®) anesthesia have been mentioned.[20b] It has been shown[15] that staphylococci mixed with blood and sucked into a syringe were not completely removed or killed by repeated rinsing in sterile water and a biniodide antiseptic solution. Mendelssohn and Witts[22] demonstrated that some blood regurgitates back into the vein when venipuncture is done by the orthodox method, thus providing a means of transferring the agent present in a contaminated syringe into the blood of the subject. Various procedures have been suggested to eliminate these outbreaks, but the simplest is to use separate syringes sterilized by dry heat at 160 C. for one hour.[23]

Extensive study of the agent responsible for serum jaundice, as well as that of infectious hepatitis, has been handicapped by the inability to transmit the disease to animals.[24] Some hope for its successful transfer to birds, however, is found in the report of Lucké and Ratcliffe.[25] Homologous serum jaundice has been successfully transmitted to human beings by intradermal, subcutaneous, intramuscular and intravenous injections,[26] at least once by feeding serum[24a] and at least once by intranasal instillation.[24b] Transmission has been possible with a dose as small as 0.01 cc.,[27] and considering the dilution of the serum in the yellow fever vaccine[11] a yet smaller dose must have been effective.

The incitant of homologous serum jaundice, as well as that of infectious hepatitis, is filtrable,[28] is resistant to heating at 56 C. in the dried state for one-half hour,[24c] can be stored for months in the dried state[29] and for three and one-half years in the frozen state[30] and can be exposed for months to 0.5 per cent of an equal mixture of phenol and ether[29] and other bactericidal agents.[31] The serum hepatitis agent is present in the blood stream before jaundice becomes manifest[29b] and apparently disappears two to two and one-half months after jaundice clears.[24a, c] It has not been recovered from the stools.[32]

The incubation period, after introduction of the serum jaundice incitant, is variable, ranging from 40 to 180 days,[33] with a majority of the cases occurring 55 to 135 days after inoculation.[33b] Reinfection with the agent of serum hepatitis, called virus SH by Neefe, Gellis and Stokes,[30] has not been described, but there have been reports of reinfection with the incitant of infectious hepatitis, or virus IH,[34] although reinfection is unusual.[30] A previous attack of serum jaundice does not produce immunity against infectious hepatitis, and there is suggestive evidence that susceptibility is actually enhanced.[35] No cross immunity between serum hepatitis and infectious hepatitis has been demonstrated,[36] which is perhaps the best evidence that there are either two different agents or two immunologically distinct strains of the same agent.

Gamma globulin has proved to be of value prophylactically in infectious hepatitis by providing complete protection or by modifying the course of the disease.[37] Data on the use of gamma globulin in serum hepatitis are inconclusive. Grossman and co-workers[38] showed that two 10 cc. injections of gamma globulin given a month apart during the incubation period were highly protective among the victims of battle casualties. A single injection of 10 cc. prolonged the incubation period without altering the disease.[39] In human volunteer experiments gamma globulin neither protected against the strain of serum hepatitis virus used nor prolonged the incubation period.[40] Oliphant[24c] found that yellow fever vaccine containing the icterogenic agent, exposed to ultraviolet irradiation, failed to produce the disease when inoculated into 10 volunteers. Wolf and co-workers,[41] using an Oppenheimer-Levinson[42] apparatus, found that irradiation produced no significant alterations of the plasma protein levels. The

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This article has been shortened in THE JOURNAL by omission of the footnotes, which will appear in the authors' reprints.

Drs. Lawrence J. Early of Hudson, N. Y., S. Gene Rogati of Valatie, N. Y., Sidney Kimelbolt of Castleton on Hudson, N. Y., and T. Frank Marnell of Great Barrington, Mass., permitted us to report the patients seen with them.

recent work of Blanchard and co-workers [43] with a Habel and Sockrider type of apparatus,[44] suggests that irradiation of plasma and serum is both safe and highly effective in preventing serum hepatitis. Inoculation of 11 volunteers with irradiated icterogenic serum failed to produce hepatitis, although it developed in 47 per cent of the control group. Allergic responses were not observed with irradiated serum and plasma.

With the increasing use of plasma and whole blood, the number of cases of homologous serum jaundice will continue to rise proportionately. When one considers an incidence of 1.6 to 7.3 per cent,[45] with a mortality rate "considerably higher" than 0.2 to 0.4 per cent,[46] the importance of serum hepatitis cannot be underestimated. That the use of pooled plasma which has not been irradiated and/or whole blood is not without danger is again brought out by the seven fatal cases here reported. An eighth case is added, even though the patient received neither plasma nor whole blood, because the peculiar contact of the victim with one of the seven patients included in this report may represent an unusual mode of transmission of the icterogenic agent.

REPORT OF CASES

Case 1.—J. F., a white man aged 39, with a known duodenal ulcer, was admitted to the hospital on Sept. 21, 1944 because of symptoms of obstruction and pain. He underwent subtotal gastric resection a week later. During the operation he was given 500 cc. of whole blood and 250 cc. of nonirradiated plasma. His recovery was uneventful, and he was discharged.

Forty-five days after the operation, an upper respiratory tract infection with fever developed. This was followed by the appearance of light stools, dark urine and jaundice. On the day of the patient's second admission, December 3, he had visual hallucinations and became confused. He lapsed into a semicomatose state shortly before he was seen in the Emergency Room. At this time his temperature was 95.2 F. and his pulse was rapid and weak. He was decidedly jaundiced and stuporous, and there was a cholemic odor to his breath. The liver was not percussible. The red blood cell count was 4.5 million per cubic millimeter; the hemoglobin was 15 Gm.; the white blood cell count was 20,000, with 69 per cent neutrophils, 27 per cent lymphocytes and 4 per cent monocytes. The urine showed bile (1 plus) and contained a few red blood cells. The blood sugar was 35 mg. and the nonprotein nitrogen 48 mg., per 100 cc. The icterus index was 67 and the carbon dioxide-combining power 28. Lumbar puncture revealed nothing abnormal in either dynamics or chemical content. The patient expired 24 hours after admission.

At autopsy the body was moderately jaundiced. The liver was much smaller than normal, weighing only 1,160 Gm. Its capsule was thin, delicate and wrinkled slightly. Through it the alternating dark reddish and paler grayish red, soft, flabby hepatic tissues could be seen. The cut surfaces showed still more clearly the alternating dark and light reddish areas indicative of extensive acute degeneration and necrosis. The appearance, save for the atrophy and flabbiness, was not unlike the nutmeg appearance of chronic congestion. The organ had the general flabby, dark red, splotchy characteristics of red atrophy.

Histologically the liver showed evidence of extensive, widespread acute hemorrhagic necrosis. Every lobule was affected. The hepatic cells were decidedly and diffusely reduced in number, and the bulk of the tissue of each lobule was severely diminished in amount. In the spaces where the hepatic cells had been there now were present accumulations of macrophages, many filled with brown pigment, neutrophils and often erythrocytes. Here and there, especially at the peripheral portions of the lobules, degenerated or necrotic hepatic cells with their cytoplasm swollen, granular and finely vacuolated still persisted, either singly or in small groups. They were usually so degenerate, and sometimes so large and filled with small vacuoles, that it was difficult to recognize them. There was no evidence of any attempts at regeneration. Because of lobular shrinkage as a result of hepatic cell necrosis, the portal zones were much closer to each other than usual, presenting the appearance of the liver of acute yellow atrophy. The portal areas, too, were diffusely infiltrated with chronically inflamed cells, especially lymphocytes. Intrahepatic bile ducts and ductules appeared to be increased in number, but this is interpreted as a relative increase only, for there was no evidence of actual proliferation of these structures. The kidneys of this patient were large and pale and histologically showed the changes of advanced tubular nephrosis, the proximal convoluted tubules being most extensively involved.

Case 2.—H. C., a white man aged 20, underwent operative intervention shortly after admission on Oct. 5, 1944 for an appendical abscess. At operation he received 500 cc. of whole blood and 250 cc. of nonirradiated plasma. The next day an additional 250 cc. of plasma was given. His postoperative course was uneventful, and he was discharged October 22.

He remained well until Dec. 14, 1944, 70 days after he received the plasma. He then began to experience chills, fever and malaise, and jaundice developed. On his admission to the hospital four days later he was acutely ill, semicomatose and jaundiced, with a temperature of 95.4 F. There was tenderness in the right upper abdominal quadrant.

His hemoglobin was 12 Gm. The leukocyte count was 16,900 per cubic millimeter; the nonprotein nitrogen was 104 mg. and the blood sugar 95 mg., per 100 cc.; the icterus index was 58 and the serum bilirubin 8.7 mg. per 100 cc. The test for bile in the urine was positive; urobilinogen was normal. He did not respond to parenterally given fluids and to oxygen therapy; he expired six hours after admission.

At autopsy the skin surfaces were all decidedly icteric. The liver was atrophic, weighing 1,460 Gm. Its edges were soft, and the organ appeared browner than is normal. Portions of the capsular surface were inflamed and covered with a thin layer of fibrinopurulent exudate. The exposed cut surfaces of sections were mottled reddish gray, congested and soft, and the stromal markings were increased. Each lobule seemed to be composed of a dark reddish center surrounded by a paler gray zone which appeared necrotic. The appearance was characteristic of diffuse necrotizing hepatitis.

Histologically the liver showed the same widespread, diffuse hemorrhagic necrosis as seen in case 1 but in an earlier stage. All lobules were affected, but many hepatic cells, either in various stages of degeneration or already necrotic, were still recognizable. Most of these were in the peripheral or middle zones of the lobules, the cells in the central portions being necrotic or massive. Also present within the hepatic cords, mixed with persisting liver cells and sometimes actually surrounding or infiltrating them, were macrophages and neutrophils. Many erythrocytes were also present, evidence of actual hemorrhage into the hepatic tissues. No evidence of regeneration could be found. Pigment deposits were relatively few and inconspicuous. Portal areas were closer together than normal, were infiltrated with inflammatory cells and contained increased numbers of bile ducts. The latter structures actually appeared to be proliferative, for their number and appearance suggested their regenerative character although actual mitoses were not observed. The kidneys were large and pale; they showed the changes of advanced tubular nephrosis, similar in type to that found in case 1.

Case 3.—E. C., a woman aged 40, a housewife, aborted spontaneously and hemorrhaged severely on Dec. 17, 1944. During her three weeks' hospitalization she had several profuse hemorrhages and was given numerous plasma and whole blood transfusions. A severe reaction followed the first blood transfusion, and it was found that she was Rh negative.

On April 30, 1945 (103 days after the patient first received plasma and blood) she complained of restlessness and became lethargic. Gradually she became comatose; progressive jaundice developed, and she was admitted to the hospital on May 2. She was in deep coma and was severely jaundiced. Her temperature was 97 F. The liver was felt 1 fingerbreadth below the costal margin. The hemoglobin level was 16 Gm., and the leukocyte count was 10,300 per cubic millimeter. The blood sugar level was 57 mg. and the nonprotein nitrogen 120 mg., per 100 cc.; the carbon dioxide-combining power was 34 volumes per cent.

The total serum protein determination was 5.8 Gm., with albumin 2.4 Gm. and globulin 3.4 Gm., per 100 cc. The prothrombin time was 150 seconds. The icterus index was 51; the serum bilirubin was 8.8 mg., total cholesterol 106 mg., free cholesterol 50 mg. and cholesterol esters 56 mg., per 100 cc. The test for bile in the urine was positive. The patient died 24 hours after admission.

At autopsy the liver of this patient was extremely small, weighing only 1,000 Gm. Its capsule was thin, transparent and smooth, and through it could be seen the pale but congested, soft, flabby hepatic tissue. On sectioning the organ the cut surfaces were found to be paler than normal; central congestion alternated with lighter bands of yellowish gray, suggestive of fatty degeneration and necrosis. Histologically, the changes in the liver were those of acute massive necrosis affecting the central and midzonal regions of the lobules and tending to affect less severely the peripheral portions. Hepatic cells were missing in the central parts of the lobules, their places being taken by inflammatory cells, particularly macrophages, some with ingested light brown pigment; lymphocytes and neutrophils were not abundant. At the periphery of the lobules, however, were periportal zones of persisting hepatic cells which showed advanced fatty degenerative changes. The degenerative cells sometimes occurred singly but were more often in small groups tending to surround the portal areas, which themselves were heavily infiltrated with lymphocytes. Intrahepatic bile ducts were not unduly prominent, and there was no evidence of regeneration of either hepatic cells or bile ducts. The kidneys, as in the other cases, were large, pale and soft and were the seat of advanced nephrotic changes which affected primarily the proximal convoluted tubules.

CASE 4.—I. C., a white woman aged 18, after tonsillectomy in another hospital on Nov. 17, 1948 hemorrhaged profusely. She went into shock and was given 1,000 cc. of nonirradiated plasma. She had a slight chill after receiving the second unit of plasma, but she made an uneventful recovery.

She began to feel ill and to have a copper tint to her skin 67 days after receiving the plasma. A week later she was found in a coma by a physician who was called to see her. She was admitted to the hospital on Jan. 30, 1948, deeply jaundiced and in a comatose state. The liver was not enlarged. The blood sugar level was 57 mg. and the nonprotein nitrogen 48 mg., per 100 cc. The leukocyte count was 12,800 per cubic millimeter. Shortly after admission she began to have convulsions, which continued until her death 24 hours later. An autopsy was not obtained.

CASE 5.—M. B., a white female infant 14 days of age, entered the hospital on Jan. 11, 1948 with a five day history of diarrhea. At this time she was acutely ill, with a temperature of 103 F., evidence of dehydration, grayish skin, and rales at both lung bases. Fluids were administered parenterally, and during the following two days small quantities of whole blood and nonirradiated plasma were given. The infant had an extremely stormy course, but she eventually recovered and was discharged 68 days after admission.

On May 8, which was 119 days after the child first received plasma and blood, she became restless and refused to eat. Vomiting followed, with evidence of abdominal pain and, later, the appearance of mild jaundice and chalklike stools. Vomiting became more profuse, and 12 days after the onset of symptoms the infant was readmitted. She appeared lethargic and moderately icteric; the temperature was 102 F. The liver was enlarged 2 fingerbreadths below the costal margin. Several convulsive seizures occurred and she grew rapidly worse, dying two hours after admission. Bilirubin was 9.6 mg. per 100 cc., and the cephalin flocculation determination was 4 plus. The urine contained bile (2 plus) but was negative for urobilinogen.

At autopsy the body was only faintly icteric. The liver appeared larger than normal, weighing 240 Gm., 50 to 60 Gm. heavier than the average weight for this age. Its capsule was smooth, glistening and a mottled yellowish brown. The organ was said to be rather firm. Cut surfaces of sections revealed large, reddish, meaty foci which oozed blood and had lost all characteristics of normal hepatic architecture. About these foci were irregular patches of pale yellowish, lobulated liver tissue which appeared degenerated or necrotic.

Histologically, the changes in the liver of this infant were those of diffuse, massive, acute degeneration and necrosis in an early stage of development. No lobules were spared. In the central regions the hepatic cells were necrotic or missing, while farther toward the peripheral portions hepatic cells showing advanced fatty degeneration were present in considerable numbers. Inflammatory cells, especially macrophages and neutrophils, were abundant though scattered, and even lymphocytes were sometimes seen. The most intense inflammation was present in the central portions of the lobules and in the portal areas, which in this case were actively inflamed. Bile ducts were abundant and in a few areas were found to be actively regenerating. Regeneration of hepatic cells was not observed. The kidneys, as in the other cases, were enlarged and nephrotic.

CASE 6.—B. M., a white female infant 10 days of age, was admitted on Feb. 9, 1948 with a three day history of diarrhea. The patient was acutely ill, dehydrated and in a state of mild acidosis. During her 46 days of hospitalization, besides the usual parenteral fluids, she was given six small infusions of nonirradiated plasma and three transfusions of whole blood without reactions. She was discharged apparently well.

On May 27, which was 105 days after the first administration of plasma and blood, the child became jaundiced. Three days later she reentered the hospital because of vomiting. At this time she was decidedly icteric and lethargic. The liver was enlarged 4 fingerbreadths below the costal margin. The blood bilirubin was 12.2 mg., the nonprotein nitrogen 72 mg. and the blood sugar 37 mg., per 100 cc. The cephalin flocculation reading was 4 plus. The patient died eight hours after admission.

At autopsy the liver was not atrophied or enlarged, weighing 176 Gm. Its surface was smooth, glistening, yellowish brown and firm. The cut surfaces of sections had an irregularly mottled appearance and small, reddish, "meatlike" foci which oozed blood alternating with pale yellowish foci. The former were regions of so-called red atrophy, while the latter were composed of degenerated hepatic tissues.

Histologically, the liver changes resembled those in the previous cases, namely, widespread, diffuse acute degeneration and necrosis. The necrosis was present particularly in the central portions of the lobules while degenerative changes, particularly of the fatty type, were noted chiefly in the peripherally situated cells that were filled with small vacuoles. Lobules generally were somewhat smaller than normal, and portal areas appeared closer together than normal. Macrophages, many of them filled with light yellow granules, and neutrophils were abundant, the latter cells chiefly in and about portal areas. Bile ducts were fairly numerous, but no evidence of regeneration of either hepatic cells or bile duct epithelium was found. The kidneys, as in all the other cases, were large, pale, and nephrotic.

CASE 7.—T. F., a white man aged 61, 90 days prior to admission received numerous blood transfusions after he underwent resection of the lower part of the colon for benign polyposis in a Boston hospital. Jaundice appeared one week before his admission here on Oct. 22, 1948 and increased rapidly. The patient became semicomatose; his temperature was 99 F., and he was deeply jaundiced. The lungs were clear. The liver was not palpable. The urine was positive for bile. The hemoglobin was 15 Gm. The leukocyte count was 19,700 per cubic millimeter. The icterus index was 150, and the direct van den Bergh reading 5.5 mg. per 100 cc. The patient was given fluids intravenously, but he remained comatose and died 24 hours after admission. An autopsy was not obtained.

CASE 8.—C. B., a woman aged 30, an undertaker's wife, was seen in consultation by one of us (R. T. B.) on June 13, 1949. A week previously she had displayed malaise and low grade fever followed by deepening jaundice, coma and convulsions. It was learned that she had assisted her husband in embalming the body of the patient I. C. (case 4) 128 days prior to her illness. Also, 68 days before her illness began she had a benign tumor removed from her right axillary region while under intravenous thiopental sodium anesthesia. However, adequate sterile technic is carried out routinely in the hospital where this latter procedure was done.

The patient was in coma, decidedly jaundiced, dehydrated and breathing rapidly. There were a few scattered coarse rales throughout both lung fields. The heart was not enlarged. The

liver was not palpable. There was slight edema over both lower extremities. In spite of parenterally given fluids and aureomycin hydrochloride, she grew steadily worse and died 72 hours later. The urine contained albumin (3 plus) and the hemoglobin was 14.5 Gm. The leukocytes numbered 6,100 per cubic millimeter. The icterus index varied from 170 to 220.

At autopsy the liver was decidedly shrunken and weighed only 630 Gm. The capsule was yellowish green, and the cut surface was deep red. Sections revealed almost complete obliteration of parenchymal cells with proliferation of the bile ducts. There was engorgement of the sinusoids with red cells and many macrophages, some of which contained yellowish brown pigment. The kidneys showed the changes of advanced nephrosis.

COMMENT

The striking characteristics of these eight cases of acute hepatitis, all but one of them occurring in patients who had received either plasma and/or whole blood from 45 to 128 days before the onset of symptoms, are the acute, fulminant nature of the illness and the fact that it progressed speedily to death within a few days. In general, the clinical course of the disease in the eight cases was similar and the duration of illness, from onset to death, was from three days in case 1 to 13 days in case 3. There was a predominance of central nervous system symptoms with psychosis (case 1), convulsions and varying states of consciousness. According to the classification outlined by Turner and co-workers,[20b] these could be grouped under subdivision one.

The precise incubation period cannot be definitely established in these cases with the exception of cases 1 and 4, because the blood or plasma was given over a period of several days or longer. The shortest possible incubation period was 45 days, the longest 128 days. These periods fall well within the reported extreme variable, but the fatal outcome would seem to bear no particular relationship to the length of the incubation period.

Five of the patients in this series received whole blood and nonirradiated plasma; the other two received either blood alone or plasma alone. The source of the icterogenic agent in case 8 is not definitely known. The development of serum hepatitis in three laboratory assistants and three orderlies handling contaminated serum has been described,[47] as well as hepatitis occurring in a blood bank worker who had received multiple needle pricks on the fingers.[19] It is quite possible that accidental inoculation took place when the body of I. C. (case 4) was embalmed. The long incubation period (128 days) is in the range of that found in serum hepatitis. Although hepatitis following intravenously given thiopental sodium is known to occur,[20b] adequate sterile technic is used in the operating rooms of the hospital where the benign tumor was removed, and it is less probable that inoculation took place at this time.

It is remarkable that six of the eight patients included in this report came to autopsy. We have been able to find in the literature [48] only scattered reports of the autopsy observations in cases of serum hepatitis. Lucké in his classic description of fatal infectious hepatitis [49] did not attempt to separate cases due to contact infection from those due to infection from blood, serum or products containing serum or its derivatives. Undoubtedly many of his cases were due to inoculation of patients with virus in blood, plasma or serum.[50] From gross and microscopic points of view, the pathologic changes in the livers of these patients were similar to, if not actually identical with, the findings reported in Lucké's monograph.

In general the liver was smaller than normal, although in at least two cases the organ was normal in size or slightly enlarged. Its surfaces were generally smooth, though sometimes wrinkled, and the color was mottled reddish and yellow or yellowish gray. The organ was generally flabby and sometimes quite soft. When sections were examined the changes of diffuse necrosis, sometimes hemorrhagic in type, were evident. The organ was sometimes bile stained, sometimes not.

The histologic changes were those of widespread acute degeneration and necrosis. In the case in which death occurred only a few days after onset, degenerative changes and necrosis of the hepatic cells predominated; in those in which death did not occur for a week or more, necrosis was advanced and many hepatic cells had already been removed, leaving only stroma and inflammatory cells. In none of the cases was any normal hepatic tissue found. Degeneration, necrosis or actual cell lysis and removal affected all the hepatic tissues.

Actual regeneration of hepatic cells and bile duct epithelium was noted only rarely in these cases, possibly because of the rapid progress of the infection to death. The histologic picture was that of an overwhelming, fulminating, hepatic-cell-destroying process which progressed rapidly to a point where all liver tissues were either degenerated or destroyed.

There is suggestive evidence that serum hepatitis from pooled plasma may be prevented by the use of ultraviolet irradiation.[51] The routine use of irradiated plasma was instituted in the Albany Hospital in February 1949. Since then there have been 10 known cases of hepatitis that have followed the administration of irradiated plasma and whole blood. This group will be reported in detail elsewhere.

As multiple injections with a single syringe and venipuncture using improperly sterilized syringes may spread the agent of serum hepatitis, these practices are not without danger. It is to be stressed that the hazards of serum hepatitis exist not only for recipients of human blood products but also for laboratory workers, technicians, nurses, physicians and undertakers.

SUMMARY

1. Seven cases of fatal serum hepatitis from whole blood and/or pooled plasma are reported, with autopsy observations in 5. An eighth case of fatal hepatitis in which blood or plasma had not been administered, also with autopsy, is added because the circumstances strongly suggest that the infection was contracted while the woman helped to embalm a person who died of serum hepatitis. Ten additional cases are mentioned in which the patients had received irradiated plasma and whole blood.

2. The pathologic changes found at autopsy in the liver and kidneys of six patients who died are described in some detail.

3. Further clinical evaluation of ultraviolet-irradiated plasma in the prevention of serum hepatitis will be necessary before final conclusions can be drawn.

4. Efforts should be made to avoid the use of a single syringe for multiple injections and the use of improperly sterilized syringes for venipuncture.

5. The potential dangers of serum hepatitis for laboratory workers, technicians, nurses, physicians and undertakers are not to be minimized, and precautions against self inoculation should be taken.

HOMOLOGOUS SERUM JAUNDICE AND ITS RELATION TO METHODS OF PLASMA STORAGE

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The infective agent responsible for homologous serum jaundice or serum hepatitis is thought to be a virus. It is transmitted by transfusion or inoculation in man by human products, particularly by blood, plasma or serum, but it has not been successfully transmitted to other species. The disease has been produced in human volunteers by as little as 0.1 cc. of infected plasma.[1] For this reason, one donor who is a carrier of the disease can infect an entire pool of plasma. It has been recommended that the donor population of pooled plasma not exceed five and that plasma be used only as an emergency measure. As a consequence, plasma is not used as extensively as before. This hazard of pooled plasma must be overcome if it is to be stockpiled and used for civilian defense.

The purpose of this report is twofold: first, to call attention to the fact that the current and generally employed methods for the storage of plasma are highly favorable to the preservation of viruses; second, to present data indicating that when plasma is stored in the liquid state without preservatives at temperatures ranging between 80 and 96 F. for three months or longer, homologous serum jaundice is infrequently encountered if indeed it occurs at all. Plasma stored in this manner for 18 to 24 months appears as effective for nutritive purposes as when stored for six months or less.

METHODS OF VIRUS PRESERVATION

The principal methods employed for the preservation of viruses are lyophilization, storage at dry ice or deep-freeze temperatures (—70 to —20 C.), refrigeration (—4 to + 4 C.) and storage in glycerin. According to Topley and Wilson[2]: "Most viruses appear to be very resistant to cold. Frozen and dried they may live for many months. Survival in distilled water, saline or Ringer's solution varies considerably. In the ice box many viruses will survive a long time, but most of them perish rapidly if kept at room temperature or 37 C." Augmenting this point of view are data we obtained from a survey of the literature on survival characteristics of 33 virus agents pathogenic for man. In every instance in which information was available, lyophilization, freezing and refrigeration favored prolonged virus survival. Storage at room temperature, on the other hand, resulted in loss of activity in a few hours to a few days even though the agent may remain virulent in the lyophilized or frozen state for months to several years.

Lyophilization, deep freezing and refrigeration, which are the best means of preserving virus activity, are also widely employed for the storage of human plasma. This may account for the persistent incidence of homologous jaundice (5 to 10 per cent) which follows transfusion of pooled plasma. A survey of the methods of plasma storage used by a number of observers reporting homologous serum jaundice following plasma transfusion discloses that in every instance the pathogenic product was stored under conditions favorable for the preservation of virus activity. Of historic and practical interest in this connection is the first reported epidemic of serum hepatitis which occurred in the Bremen shipyards in 1883. Vaccination for smallpox with human lymph stored in glycerin resulted in latent icterus in 191 of 1,293 persons treated.[3]

A review of the literature available to us discloses that homologous serum jaundice has been reported[4] from plasma or serum preserved as shown on table 1. It is clearly evident from this table and from the literature pertaining to the survival qualities of other viruses that if the blood product is to be stored in the lyophilized, frozen or refrigerated states it must first be free of all virus contaminants. Failing this, these products must be stored for an undetermined period of time under some condition which is unfavorable for virus preserva-

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Sponsored by the Medical Research and Development Board, Office of the Surgeon General, Department of the Army.

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tion. If the latter procedure is followed, the method of storage must not destroy the activity of the product as far as its therapeutic value is concerned.

HOMOLOGOUS SERUM JAUNDICE AT THE UNIVERSITY OF CHICAGO CLINICS

BLOOD TRANSFUSION

As the members of the medical profession became generally aware of the possibility that delayed jaundice after transfusion was due to the transmission of a virus contained in the transfused human product, they began to make the diagnosis of homologous serum jaundice in patients in whom there developed latent icterus after transfusion. During the past eight years 33 of our patients have returned with jaundice and this diagnosis has been made. Sixteen of this group had either a previously established primary liver disorder or metastatic liver tumor and are therefore excluded from this series unless biopsy or autopsy evidence of hepatitis

TABLE 1.—*Homologous Serum Jaundice and Method of Plasma Storage*

Method of Storage	Number of Reports
Glycerinized human lymph [3]	1
Refrigerated (footnote 4, parts a to e, inclusive)	9
Frozen (footnote 4, parts d, f, g and h)	7
Lyophilized (footnote 4, parts b and i to k, inclusive)	18
Prolonged room temperature storage	
(a) In lyophilized state [4d, 1]	2
(b) In liquid state	0
Total number of reports reviewed	37

TABLE 2.—*Data Relative to Blood and Plasma Transfusions from Sept. 15, 1942 to June 1, 1950*

Type of Transfusion	Total No. of Units Transfused		Average No. of Donors of Plasma Each Patient Received		Known No. of Patients in Whom Homologous Serum Jaundice Developed	No. of Patients Transfused
Blood only	23,320		3.3		14	6,503
Plasma only	1,356		44		0	212
Blood and plasma	Blood 3,532	Plasma 5,000	Blood 4.8	Plasma 48	3	632

could be established. None of these 16 patients had received our University of Chicago plasma. The remaining 17 patients are considered as having acquired the disease, and their cases are reported below and summarized in table 2.

CASE 1.—A. C., a man aged 47, had chondrosarcoma of the ilium and bleeding duodenal ulcer. He was admitted Jan. 15, 1950 and was transfused with four units (1,000 cc.) of our plasma on the same day. This was from two separate pools. The ages of these pools were 145 days and 182 days at the time of administration. The total donor population of these two pools was 60. Thereafter the patient was given whole blood, 2,000, 1,000, 3,000 and 2,000 cc., respectively, on January 16, 17, 19 and 20, on which day a subtotal gastrectomy was performed. Subsequent transfusions were as follows: 3,250, 500, 500 and 500 cc. on January 21, 26, 28 and 31, respectively. He was discharged in good condition February 19 and readmitted March 26, 1950 with nausea, vomiting and anorexia accompanied with jaundice of three days' duration. Diagnosis of homologous serum jaundice was made, and he recovered. In all he had received blood transfusions from 39 donors and four units of our plasma. Requestioning of donors used for blood transfusion disclosed that two of them had had symptoms of jaundice. The remaining units of these plasma pools were given, in one instance to 17 patients as 250 cc. units and in the second case to eight patients as 500 cc. units. These patients were reexamined but no evidence of jaundice or symptoms of hepatitis developed, although two had died within less than two months of other disease.

CASE 2.—M. A., a woman aged 48, was admitted with a diagnosis of ulcerative colitis. In 1948 she received blood transfusions on March 5, 23, 24, 25 and 31, April 1, 2, 3, 4 and 20, May 17 and 25 and June 20 and 22. She received one 500 cc. transfusion of our plasma on March 24 with a donor population of 34 donors. The age of this plasma unit was 143 days. Thereafter she was given war surplus lyophilized plasma on March 25, 26, 27, 28, 29, 30 and 31, April 1, 2, 3, 4 and 5 and 1,200 cc. on April 6 and 7. On August 21 symptoms of hepatitis began. Jaundice was noted the following day. The patient became oliguric but began to improve September 1, although icterus was present until September 16. She was discharged on her forty-third hospital day (October 10) and has remained well since. In all, 11,000 cc. of lyophilized plasma were given. The remaining units of our plasma pool were given to nine patients who were followed for six months but in whom symptoms of hepatitis or jaundice did not develop; one other patient receiving this plasma died two weeks later of other disease.

CASE 3.—J. M., a man aged 19, whose diagnosis was trabecular reticulum cell sarcoma of the left iliofemoral chain of glands, had an operation for excision of this chain of glands with resection of external iliac and proximal portions of superficial and deep femoral veins on June 22, 1949. During the operation he received four transfusions of whole blood and four units of our plasma from two different pools whose combined donor population was 55. The ages of the plasma units were 215 and 392 days. An additional 500 cc. blood transfusion was given July 5, and recovery was uneventful. The patient was discharged on August 20 and readmitted October 12 with a 10 day history of jaundice, anorexia, nausea and some vomiting. This slowly improved over a period of three weeks. Two needle biopsies of the liver were done and showed severe hepatitis. One performed October 15 and a second performed October 29 disclosed considerable improvement since the first examination. One of three blood donors who were recontacted gave a history of jaundice 40 years before. The other two donors did not return. The remainder of each plasma pool was administered as 500 cc. units to six patients and eight patients, respectively, in none of whom symptoms of hepatitis had developed within a six month follow-up period.

CASE 4.—K. H., a woman aged 82, was first admitted to Billings Hospital in November 1948 and was found to have a gastric ulcer. Subtotal gastrectomy was done Dec. 8, 1948. She received two whole blood transfusions preoperatively, one on November 27 and one November 28. On February 1 jaundice developed. This progressed until the death of the patient. Necropsy disclosed evidence of hepatitis.

CASE 5.—F. S., a patient aged 64, was admitted January 2, 1950 with carcinoma of rectum and sigmoid with intestinal obstruction. A combined abdominal-perineal resection was done and three transfusions totaling 1,650 cc. of blood were given. Three blood transfusions were also given January 5, 12 and 26 during the postoperative period. On March 10 the patient manifested painless jaundice with acholic stools and anorexia but without fever. This subsided after three weeks, and since then the patient has been well. Plasma was not given.

CASE 6.—C. J., a man aged 64, underwent operation for pyogenic arthritis of two joints on April 29, 1944. Two days prior to operation, one transfusion of whole blood was given. Four weeks later a transurethral resection was done because of benign prostatic hypertrophy. Seventy-two days after the transfusion the man was readmitted because of headache and dizziness. Two days later he became comatose, bleeding from the nose and intestinal tract; he died on the third hospital day. At autopsy the liver weighed 1,300 Gm. and was yellow with increased prominence of globular markings. Microscopic examination revealed fine granular fat dispersed throughout the entire liver section with nearly complete destruction of the lobular architecture, except in the periportal areas where abortive attempt at regeneration was evident. Numerous round cell infiltrations were evident throughout the liver lobules and periportal areas. The blood donor was requestioned, but no history of hepatitis could be elicited. Plasma was not given.

CASE 7.—P. S., a man aged 70 with a squamous cell carcinoma of the skin, underwent operative intervention on Dec. 2, 1944, and 600 cc. of blood was given at that time. Two other blood transfusions were given, one on December 18 and one on December 26. On May 1, 1945 the patient had symptoms of hepatitis with mild icterus and lack of appetite; he required three weeks' hospitalization. Complete recovery was made. A history of previous hepatitis was not elicited from the donors. Plasma was not given.

CASE 8.—E. M., a woman aged 50, was admitted with a diagnosis of Hodgkin's disease on Jan. 31, 1947. One blood transfusion was given March 13, and the patient was discharged March 16, 1947. Jaundice was first noted July 28, 1947, preceded by anorexia of ten days. No treatment of Hodgkin's disease was actively conducted for three months before the onset of jaundice. The jaundice receded and disappeared with restoration of appetite by August 14. The patient made a recovery from hepatitis and is still alive. Plasma was not given.

CASE 9.—H. B., a man aged 72, was given three blood transfusions for anemia, one on Nov. 5, 1946, the second on November 19 and the third on December 17. Onset of hepatitis with icterus occurred March 5, 1947. The patient recovered after three weeks. Subsequently one blood donor gave a history of jaundice three months before giving blood for this patient. Plasma was not administered.

CASE 10.—A. C., a woman aged 53, her condition diagnosed as Hodgkin's disease, was given blood transfusions on January 15, 17, 18 and 21 in 1949. She was readmitted to the hospital March 14, 1949 with jaundice, nausea and vomiting. She was given a course of nitrogen mustard therapy totaling 28.8 mg., started March 30. She continued to go downhill, although jaundice cleared. She expired on April 7, 1949. Plasma was not given. Liver sections showed a decided increase of portal fibrous tissue without extension to form lobular divisions. Only occasionally was Hodgkin's disease in evidence. Leukocytes and round cell infiltration were present in most areas.

CASE 11.—R. W., a man aged 60, was admitted Nov. 21, 1947 with pyogenic arthritis. Blood transfusions were given November 26, and December 6, 9 and 11. On March 8, 1943, the urine darkened and there developed nausea, lack of appetite and jaundice. This gradually cleared up over four weeks' time, and the patient was well as of April 19, 1950. Plasma was not given.

CASE 12.—F. H., a man aged 64, with a diagnosis of carcinoma of the descending colon, underwent operation on Dec. 16, 1948 and received two units of blood. His convalescence was uneventful, and he was discharged on the twelfth day. He was readmitted May 8, 1949 with onset of anorexia, nausea, vomiting and jaundice of three days' duration. Needle biopsy of the liver was compatible with hepatitis; the diagnosis was presumed to be homologous serum jaundice. The patient improved, and he was discharged at the end of two weeks and is well at present. He did not receive plasma.

CASE 13.—E. G., a woman aged 47, with a diagnosis of chronic lymphatic leukemia, received five blood transfusions between Sept. 15 and Dec. 20, 1949. Anorexia, nausea and icterus developed on Jan. 28, 1950. Donors were interrogated but without revealing any possible source of infection. Her course in the hospital was uneventful and her recovery from hepatitis was complete. During this hospital stay she did not receive antileukemic therapy. Plasma was not given.

CASE 14.—L. G., a woman aged 60, with a diagnosis of carcinoids of small intestine, received five blood transfusions beginning on October 4 and ending November 7, 1949. No plasma was given. On Jan. 15, 1950 the patient developed anorexia, nausea and vomiting, and within a day or two, jaundice appeared which subsided spontaneously over a period of three to four weeks. Interrogation of the blood donors disclosed no evidence of previous hepatitis.

CASE 15.—J. S., a man aged 60, was admitted with a diagnosis of duodenal ulcer. He received three blood transfusions Dec. 15, 1947 in the treatment of an acute episode of gastrointestinal bleeding presumed to be from a duodenal ulcer. No plasma was given. He was admitted for surgery on March 15, 1948 and, on the day surgery was planned, icterus was noted. Aside from jaundice, the patient was otherwise asymptomatic. Jaundice cleared in three weeks. No surgery was performed. Investigation of the donors did not disclose the source of infection.

CASE 16.—E. F., a woman aged 60, was admitted March 19, 1950 with a diagnosis of hypernephroma of the left kidney, an adenoma malignum of the descending colon and diabetes mellitus. On March 27 the left kidney was removed and a local resection of the descending colon was performed. She received one 500 cc. blood transfusion March 22 and two blood transfusions of 500 cc. each March 27 during operation. Her recovery was uneventful, and she was discharged April 9. She was readmitted May 6, 1950 complaining of anorexia, nausea, generalized pruritus and jaundice of three to ten days' duration. A diagnosis of homologous serum jaundice was made, and conformation of hepatitis was obtained by needle biopsy of the liver. Jaundice subsided, and she was discharged May 18, 1950. The three donors were recalled, but no history of hepatitis or jaundice was obtained. Plasma was not given.

CASE 17.—V. S., a woman aged 33, on June 21, 1950 had a cesarean hysterectomy with right salpingo-oophorectomy. Her course was complicated by pelvic vein thrombosis. She received one 500 cc. blood transfusion on the day of surgical intervention. Her recovery was otherwise uneventful, and she was discharged July 6 in good condition. She was readmitted on July 25, 1950 with complaints of epigastric distress, anorexia, nausea and vomiting of less than one week's duration. Homologous serum jaundice was suspected, and the diagnosis of hepatitis was confirmed by needle biopsy. Her course improved and jaundice disappeared by August 12. She was discharged on Aug. 15, 1950. She did not receive plasma. On requestioning the donor, no history of hepatitis or jaundice was obtained.

PLASMA TRANSFUSION

Save for the three patients whose clinical summaries are presented in case reports 1, 2 and 3, we have not encountered any other patients receiving our plasma who are known to have had the homologous serum jaundice syndrome. Although our plasma cannot be completely excluded as the cause of infection in these three patients, it seems more likely that whole blood or lyophilized plasma was the icterogenic agent concerned. In support of this contention are the important facts that in none of the other 39 patients receiving the remaining plasma units from these pools did there develop recognizable latent hepatitis or icterus and that at least one blood donor to each of these three patients gave a history of previous hepatitis and jaundice.

Because of the relatively large number of patients transfused, 6,503 with blood alone and 864 with our plasma with or without blood, we believe that we should have encountered some definite evidence of transmission of the disease by our plasma unless the unusual means of its storage influenced the virulence of the virus. The method of our plasma preparation from the beginning of the Blood Bank, Sept. 15, 1942, has been the same and is as follows:

Plasma is prepared from outdated blood (five days or older). It is separated from the sedimented red cell mass and thereafter stored at room temperature until used. Each blood transfusion is drawn into a 75 cc. aqueous solution of sodium citrate (2 Gm.) and is stored at refrigeration temperatures (4 to 8 C.) until transfused as such or converted into plasma, pooling generally with plasma from 25 to 30 other donors. After five days all bloods are made into plasma. This plasma is stored at room temperature without preservatives.

The temperature of the room in which the plasma is stored is higher than might be expected, as the liquid plasma is stored within 2 feet of the ceiling and is in the same room where blood bank equipment is autoclaved. In addition, a 30 gallon steam still also is located there and is in continuous operation 12 hours a day, six days a week. Temperatures recorded during

the winter seasons are regularly 78 to 82 F. The temperature is more variable during the seasons of late spring, summer and early autumn, when the room temperature is a function of the weather. In the interest of economy of space, representative daily room temperature readings are not included. Storage of plasma under these conditions was originally begun because refrigeration facilities were not available when our blood bank was started in 1942. This practice has been continued because it has proved satisfactory.

TABLE 3.—*Age Distribution of Plasma Transfused*

Age in Days	Units Transfused	Age in Days	Units Transfused	Age in Days	Units Transfused	Age in Days	Units Transfused
25-44	10	95-124	650	235-394	378	935-1 054	14
45-54	60	125-154	768	395-454	220	1,055-1,174	4
55-64	170	155-184	778	455-514	90	Not recorded	80
65-74	250	185 214	712	515-574	74	Total	6,502
75-84	320	215-274	1,130	575-754	114	.....	...
85-94	302	275-334	262	755-934	36	.....	...

From Sept. 1, 1942 to June 1, 1950, a total of 864 patients received 6,502 of the 9,406 units of blood from which 356 pools of plasma were made. Samples from all these pools have been administered, although some units until recently were discarded after the one year arbitrary expiration date. Many of these patients received plasma from several pools and were thus exposed to a fairly large donor population. The average donor population of each pool was 26. Each patient received, on the average, plasma from 44 donors because generally more than one unit of plasma was given, and often these units were from different pools.

From the beginning of our blood bank, an attempt was made to restrict the administration of any pool of plasma until it had aged two to three months, in order that some deterioration in isoagglutinin titer might occur. Except when clinical demands were great, this was usually possible. Table 3 records the ages of all the various units of plasma at the time of administration.

An analysis of the end results of plasma transfusion with reference to the occurrence of homologous serum jaundice had to be the subject of search of each patient's clinical record, as no patients with this complication from our plasma had come to the attention of either the attending service or the blood bank. This record search was extended to include also most of those patients who had received only blood. Thirteen of the 14 patients receiving blood only had been called to our attention by the attending service. Only one patient (case 11) was brought to light by the record search.

TABLE 4.—*Number of Records of Patients Receiving Transfusions That Were Reviewed and Duration of Follow-Up*

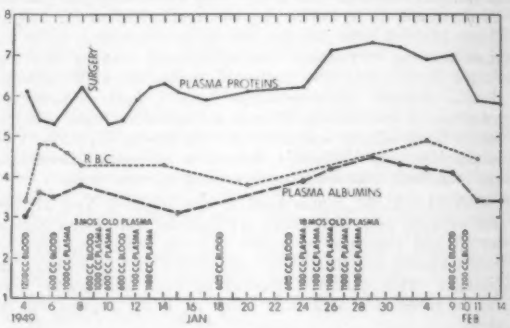
	1 Mo.*	1 Mo.	2 Mo.	3 Mo.	4 Mo.	5 Mo.	6 Mo.†
Blood only							
No. of records.....	508	840	452	285	233	458	2,700
Percentage of total.....	9.1%	15.1%	8.1%	5.1%	4.2%	8.2%	50.1%
Blood and/or plasma							
No. of records.....	71	26	53	54	73	97	480
Percentage of total.....	8.2%	4.2%	6.1%	6.3%	8.4%	11.2%	55.6%

* Died or followed less than 30 days. † Six months or longer.

Of 7,367 patients transfused with blood and/or our plasma, 5,566 records of patients receiving only blood were reviewed. All the charts of the 864 patients receiving our plasma were reviewed. Nine hundred and thirty-seven charts were either in active clinic use or had been microfilmed and were not available at the time the survey was made. The charts of the 864 patients who received plasma were reviewed later for a second time. The length of the follow-up period for each patient was tabulated, and these data are presented in table 4.

The over-all incidence of homologous serum jaundice for pooled plasma is reported by various workers as between 2.4 and 12 per cent of the patients transfused. Perhaps the most reliable estimate made in this country is the careful survey of Brightman and Korns [4] in which at least 29 of 649 patients receiving war surplus lyophilized plasma were considered to have contracted the disease. The incidence of the disease is much higher (23 to 100 per cent) when computed on the basis of the patients receiving units from any one infected pool (table 1).

A number of possible mathematical means may be employed for estimating the number of patients receiving our plasma in whom homologous serum jaundice could be expected to develop, but none is without the criticism that the data would be handled with some arbitrary advantage. The basic facts in our data are: first, 23,320 whole blood transfusions were given to 6,503 patients; second, 9,406 plasmas were pooled into 356 pools, so that each final plasma unit contained on the average 26 donors. Of this plasma, 6,502 units were given to 864 patients, who on the average received plasma from 44 donors based on an analysis of the individual's plasma transfusion record as the plasma was actually given. Of this latter group, 212 patients did not receive blood in connection with their plasma therapy. The homologous serum jaundice syndrome appeared in 14 patients receiving blood alone. Three more patients, given both blood and our plasma, also exhibited this syndrome, although in each of these three patients it seemed unlikely that our plasma was the cause of their infection. None of the 212 patients who received our plasma alone were known to have manifested the disease.



Response of plasma protein concentration to administration of plasma stored 18 months at room temperature, unit 460129. Protein level is shown in grams per 100 cc., red blood cells in millions per cubic millimeter.

NUTRITIVE VALUE OF PLASMA STORED AT ROOM TEMPERATURE

Because plasma is slowly metabolized it is the most valuable and effective means available for providing the patient with parenteral protein.[5] The accompanying illustration presents data which shows the capacity of plasma to elevate the plasma protein concentration after

5. Allen, J. G.; Egner, W.; Brandt, M. B., and Phemister, D. B.: Use of Blood and Plasma in Correction of Protein Deficiencies in Surgical Patients, Ann. Surg. **131**:1, 1950.

it has been stored 18 months to two years at room temperature in the liquid state. In two other instances this plasma was the only plasma administered, and similar responses in plasma protein concentration were achieved. Metabolic studies were performed and satisfactory positive nitrogen balances were obtained. The plasma protein responses were essentially the same as reported in previous studies from this laboratory, in which the plasma administered had been stored at room temperature for three to twelve months before use.[6]

COMMENT

To one who is cognizant that lyophilizing, freezing and refrigeration are the best means available for the preservation of virus activity, it is not surprising that when these same procedures are employed in the preservation of plasma the activity of the virus of homologous serum jaundice should also be preserved. The question arises, however, if this is true why are other virus diseases not transmitted under these same conditions? The answer probably lies in certain characteristics almost unique with the virus of homologous serum jaundice. Most other viruses pathogenic for man are present in the blood stream only a few days, and during this time the person is ill and therefore does not give blood. The virus of homologous serum jaundice, however, can be present in the blood stream for many weeks and at a time when the person is in apparently good health; hence, these persons are not rejected as donors.

Another pertinent problem concerns the known ability of the virus of homologous serum jaundice to resist various forms of physical exposure. For example, it is known that this virus will resist temperature of 56 to 60 C. for at least 30 minutes; that it will survive temperatures of 4 C. for long periods of time and temperatures of — 10 to — 70 C. for one to two and a half years.[7] At room temperature, but in the lyophilized state, the virus maintains its activity for at least a year.[1a] It also survives in serum, refrigerated or frozen, with or without thimerosal (merthiolate®) concentrations of 1:1,000 to 1:2,000 with equal parts of phenol, and it maintains its activity in 0.5 per cent ether and in 0.2 per cent concentrations of tricresol at similar temperatures.[7] It is inactivated by exposure to ultraviolet light and heating at 60 C. for 10 hours. This virus is one of the most stable and resistant of all known viruses.

With these points of view in mind, is it possible that the virus of homologous serum jaundice can be inactivated simply by prolonged storage in a liquid cell-free state, in a temperature environment of the type employed in this report? According to Havens [7] the virus may remain virulent in the lyophilized state for one to four and a half years but becomes inactive after five years. Undoubtedly, if the virus will "die out" after prolonged storage under conditions favorable to virus activity, it will "die out" more rapidly under less favorable conditions. Our data suggest that the virus of homologous serum jaundice does not remain pathogenic in liquid cell-free plasma at temperatures ranging between 78 and 96 F. for more than three months. However, if this is true, the data do not tell us the minimum temperature or storage period at which this apparent inactivation occurs.

Since this study rests entirely on data obtained from a record search and from complaints of previously transfused patients, it is open to the criticism that a personal inquiry into the subsequent course of each patient with reference to possible latent homologous serum jaundice was not made. Undoubtedly, some patients were missed in a project of this magnitude. On the other hand, 14 patients who received only blood, five days old or less, manifested a syndrome that seemed compatible with homologous serum jaundice. Since nearly one fourth of all of our blood was converted into plasma, each pool containing on the average the blood of 26 donors and the average patient receiving a total plasma donor population of 44, it is evident that we could expect some homologous serum jaundice to develop from plasma. This does not appear to have happened. These observations differ from those of all other investigators "who have found the incidence of hepatitis following pooled plasma transfusion many times greater than following transfusion of blood." [4g]

There is no reason to suspect that the patients who received our plasma were immune to homologous serum jaundice, or, for that matter, immunized against a return to our clinic to an extent greater than were those who received our whole blood. The only logical conclusion is that the susceptibility to homologous serum jaundice from our plasma was less than that from our whole blood. As far as we know, this is the only report in which the incidence of homologous serum jaundice following plasma transfusion was less than that following blood transfusion.

Although it is reasonably certain that the 17 patients whose cases are reported herein had hepatitis with jaundice, it cannot be stated that in every instance the jaundice and hepatitis were transmitted by blood. The possibility of sporadic or endemic infectious hepatitis as the primary cause of their disease cannot be excluded. It is not yet possible to distinguish accurately between homologous serum jaundice and endemic hepatitis in patients who have received parenteral human products. However, since all the previous reports also are open to the same criticism, we believe that this objection has no special significance in connection with our data.

It appears likely that the incidence of homologous serum jaundice as indicated by our record search is a minimum figure, for undoubtedly some of our patients in whom latent icterus developed were treated elsewhere or failed to report for medical attention at all. It must be borne in mind in estimating the incidence of any infectious disease that the results obtained are measured in terms of the resistance of the host and the virulence of the organism. The absence or low incidence of the disease in patients receiving our plasma was probably the result of a reduced virulence of the organism rather than an increased resistance on the part of the patient, since the disease did occur following transfusions of whole blood. No evident case selections were in function to determine which patients should receive blood and which should receive plasma. It is our belief that if storage of liquid plasma at relatively high room temperatures for at least two to three months does not cause the death of the virus its virulence is reduced to the extent that few if any patients receiving such plasma manifest the disease.

"Sterilization" of plasma or serum containing viruses may be accomplished by a number of methods besides prolonged storage of the liquid cell-free product at room temperature. Chief among these are exposure to ultraviolet light, certain ionizing radiations and chemical agents, especially nitrogen mustard. Until all the factors concerning the toxicity and the safety of this prac-

6. Allen, J. G.; Bogardus, G.; Egner, W., and Phemister, D. B.: Correction of Hypoproteinemia by Administration of Plasma and Blood, Surg., Gynec. & Obst. **86**: 604, 1948. Allen, Egner, Brandt and Phemister.[5]

7. Havens, W. P., Jr.: Infectious Hepatitis, Medicine **27**: 279, 1948.

tice are known, its use beyond that of clinical investigation should not be encouraged. The use of plasma irradiated with ultraviolet light has not completely eradicated the problem of homologous serum jaundice. This may be corrected when the light energies necessary to kill the virus without impairing the physiologic value of the plasma are known and such information employed as routine procedure. Objections of similar nature apply to the prolonged storage of liquid plasma at high room temperature, because neither the optimal temperature or minimal storage period for inactivation of the virus are established. Our data do not prove that room temperature storage under the conditions we report actually kills the virus, but if it does not the resistance qualities of the virus of homologous serum jaundice would be unique in this respect. For these reasons, we do not contend that the prolonged room temperature storage of liquid plasma should be generally practiced as a means of preventing homologous serum jaundice at present, although our data suggest that this is a simple and safe method for reducing or abolishing the incidence of homologous serum jaundice from pooled plasma.

In the past eight years this plasma has been successfully employed in the emergency treatment of shock. Precise comparison with plasma stored under other conditions is not possible from our experience, but we have no clinical observations to indicate that our plasma is unsatisfactory in this respect. The criticism that plasma stored at room temperature could be a means for the transmission of bacterial contaminants is, in our opinion, not justified. It is true that plasma or serum stored under these conditions is an ideal culture medium for many organisms. In our experience, when bacterial contamination occurs one or more of several phenomena are readily noticeable: the plasma becomes turbid and may develop a flocculum; it may coagulate and often is rapidly discolored, and if gas is formed by the organism the stopper is frequently blown off the bottle. Contaminated plasmas can generally be recognized and set aside even before the routine culture data from the bacteriologic laboratory have been reported.

Liquid proteins generally are denatured on prolonged storage at room temperature. It is inconceivable that plasma as we have stored it does not undergo some changes of this sort. Nevertheless, such changes as may occur do not appear to impair the nutritive capacity of such plasma. On no occasions did the three patients receiving 18 to 24 months old plasma exhibit any untoward reaction. In all, 81 units of "old" plasma were administered to these three patients. The over-all reaction in our clinic to blood transfusion is 2.8 per cent compared to 0.4 per cent for our plasma.

A study of the physical and chemical qualities of liquid plasma stored at room temperature from three months to eight years is in progress and will be the subject of a later report.

SUMMARY

1. Lyophilization, freezing and refrigeration, almost exclusively employed in the preservation of plasma, are also the most suitable means available for the preservation of virus activity. As long as these methods are employed for the storage of plasma, it is imperative that pooled plasma be sterilized in some manner before such storage procedures are instituted in order to reduce or obviate the troublesome incidence of homologous serum jaundice from pooled plasma.

2. No virus is known to survive prolonged room temperature in a cell-free liquid state without preservatives. In the University of Chicago Clinics, where plasma has been stored at high room temperature for a period of three to 12 months before use, it appears doubtful that any patient has contracted homologous serum jaundice from this plasma. Of 864 patients given units of our pooled plasma stored in the liquid state at 78 to 96 F. for three months or longer, three are known to have contracted homologous serum jaundice. The source of infection in these three patients seemed more likely due to the blood received by two of them or to the lyophilized plasma or blood given the third patient. None of the 212 patients who received our plasma alone was known to have had latent jaundice. This plasma appears undiminished in its nutritive value and is remarkably free of elements causing untoward reactions.

3. During the same period, at least 14 and probably 16 or 17 of 6,503 patients receiving only refrigerated whole blood transfusions manifested latent jaundice typical of the homologous serum jaundice syndrome. Case abstracts of these 17 patients are reported.

OCCURRENCE OF HEPATITIS IN RECENTLY TATTOOED SERVICE PERSONNEL

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I shall attempt to demonstrate in this paper a possible relationship between tattooing and hepatitis. A perusal of the literature up to June of 1949 failed to reveal any mention of the subject of tattooing in hepatitis, hence, a report at this time is all the more pertinent. In the absence of the actual reproduction of the disease in human volunteers with material from a suspected reservoir, positive proof can never be offered and all conclusions must be based on deduction, elimination and supposition. All the data were obtained from the medical service of Fort Clayton Hospital, Fort Clayton, Canal Zone, where enlisted patients of the three services were observed. Results of the study thus far on the subject of tattooing and hepatitis have been considered of sufficient weight already to warrant preventive measures against another possible mode of dissemination of hepatitis, just as hospital technic has been altered in the past five years to prevent transfer of the hepatitis virus through supplies, not only in blood products but also in needles.[1]

SERUM HEPATITIS AND INFECTIOUS HEPATITIS

The etiological agent in the two forms of homologous serum jaundice, infectious hepatitis and serum hepatitis, is as yet unidentified. Electron microscopic examinations of filtered extracts of proved infected serum have disclosed nothing. Implantation on the chick embryo has produced no consistent or reproducible lesions.[2] Inclusion bodies have not been found by the pathologist in studies of patients with hepatitis.[2] However, because of the ability of the etiological agent to pass through bacteria-retaining filters, it would seem that the name virus would be most applicable to the causative agent.

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With the assistance of Col. W. D. Graham, commanding officer, Fort Clayton Hospital, and Lieut. Col. Norman Elton, chief, Board of Health Laboratory, Gorgas Hospital, Ancon, Canal Zone.

1. Cappa, R. B.; Sborov, V., and Scheifley, C. H.: Syringe-Transmitted Epidemic of Infectious Hepatitis, with Observations Regarding Incidence and Nature of Infectious Donors, J. A. M. A. **136**: 810 (March 20) 1948.

2. Hepatitis, Combined Staff Clinics, Am. J. Med. **4**: 285, 1948.

Considerable experimental work has been done in an attempt to prove or disprove the theory that the viruses in infectious and serum hepatitis are one and the same. In support of the theory it is stated that the etiological agents are equally elusive, filtrable and resistant, as well as productive of identical changes in vivo. Aycock and Oren [3] showed that by giving the virus of infectious hepatitis parenterally to 22 volunteers a prolonged incubation period resulted, averaging 61.6 days. They deduced that this tended to substantiate a common cause for both diseases. They went on to state that the probable cause for the longer incubation period of serum hepatitis was either partial inactivation of the virus by human serum or inoculation of virus from a convalescent or abortive case. Neefe and his co-workers,[4] doing original work, and Haggard,[5] expertly summarizing the experimental work, have forcibly contended that a different agent is causative in these two diseases. Their conclusions are based on the fact that cross immunity does not exist between the two kinds of hepatitis. This has been well established not only in experimental infections but also in the numerous large wartime series of cases.

Actually, the only differences between the two diseases are the mode of transmission and the incubation period. Serum hepatitis is transmitted parenterally with a 40 to 160 day incubation period and infectious hepatitis orally with a 15 to 40 day incubation period. Clinically, there is no symptomatic, laboratory or duration difference that may be applied to the individual case.[6] When differences in the two diseases have been found, there have been other factors, such as the older age in serum hepatitis in the peacetime series or the battle wounds which were a concomitant in many other wartime series. The lack of ability to differentiate has been true of the cases which will be discussed in this paper.

Probably the most significant factor about the viruses of hepatitis which has fostered perpetuation of the disease has been their extreme hardiness in the presence of measures which usually are effective in eradicating bacterial disease. Environmental extremes are not deleterious to the viruses, as they survive several years in the frozen state and at least a year when desiccated at room temperature.[7] A high level of resistance to thimerosal (merthiolate®), equal parts of phenol and ether, alcohol and a temperature of 56 C. for 30 to 60 minutes has been shown. One of the few practical effective measures for destroying the virus in blood products is irradiation with ultraviolet light for 45 minutes at 2,537 angstrom units.[8] Boiling for 30 minutes is effective but only applicable in instrument sterilization.

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TATTOOING AS MODE OF TRANSMISSION

The impetus of this investigation came about in July 1949 when it was noted on making rounds on the enlisted male medical ward that the most decorative section seemed to be the one reserved for patients with hepatitis. On closer scrutiny the reason became apparent. The tattooed males were predominant in this section. Many of these patients had been tattooed within two to five months prior to onset of symptoms, and this cutaneous glorification had been performed most commonly at the same establishment in Panama City.

Twenty-six cases of hepatitis were followed in this series. All patients were included who had hepatitis occurring after January 1949 and could be called back for further questioning or who came into the hospital after the study began. The patients were asked whether, when and where they were tattooed. They were questioned about past history of jaundice or contact with jaundiced persons, whether they had been hospitalized within the past six months and, most important, whether they had received any blood transfusions or plasma within the past year. Because of the time elapsing between the tattooing and the symptoms, often the incubation period was approximated to the nearest week.

It was found that 18 of the 26 men, or 69 per cent, had been tattooed 49 to 154 days prior to the onset of their symptoms. All tattoos which were done outside the 40 to 160 days were not considered as a possible cause of the serum hepatitis. Three of the patients had had more than one tattoo. Each had had at least one tattoo within the incubation period. All 18 patients denied contact with any jaundiced persons. Seventeen of the 18 had been tattooed at the same establishment. Two had been tattooed the same night at the same place and entered the hospital during the same week for therapy. They knew of no other likely contact, mutual or otherwise. In these two patients the clinical courses were quite different, one being much more deeply jaundiced and thereby requiring protracted hospitalization. In another patient who was hospitalized for a fractured nose hepatitis developed in the fourth week of his hospitalization. He gave a history of being tattooed 65 days prior to symptoms. The average time elapsing between tattooing and symptoms in the 18 patients was 99 days.

All the patients were returned to duty within three months with no evidence of impaired liver function. Each was checked one month after discharge, and only one patient required rehospitalization. No clinical or laboratory difference was evident between the 18 patients with significant tattoos and the other eight patients.

Because the incidence of tattooing is known to be high among service personnel, hospitalized enlisted men were questioned on this subject at three separate times until a total of 200 cases were obtained. The only patients excluded were the hepatitis patients in the hospital at these times. Sixty-one patients (30 per cent) were found to have had tattoos. Sixteen (8 per cent) of these patients had been tattooed at the establishment previously mentioned. None of these 16 gave a history of jaundice, but two had hepatomegaly; however, both had normal hepatic function tests. This comparison in tattoos in the nonhepatitis series of 30 per cent and total tattoos in the hepatitis series of 88 per cent seems to constitute a significant difference.[9]

9. In the series of 26 cases were 18 patients with significant tattoos and 4 who were tattooed outside of the average incubation period of serum hepatitis.

The next step taken was to study the tattooing methods locally used and to ascertain whether the technics might be conducive to virus propagation. The procedure disclosed was as follows: The skin was shaved and washed with alcohol and allowed to dry. Then the stencil of choice was dusted with fingerprint powder and applied to the skin. After removal of the stencil the pattern was "needled in" with from two to four colors. The colors were kept in separate containers. All transfer to the patient from the container was by direct "dips" of the tattoo needles. A tattoo needle consists of a battery of four or five needles in a row, attached to a vibrator. A separate needle battery was used for each color. When the material at the end of the first dip had been used up on the skin, the needle was redipped into the dye container. The process was continued until the pattern was completed. Between customers, the needle was wiped with a cotton rag and dipped into a 3 ounce (90 cc.) alcohol bottle and allowed to dry. When the dye in the working container became depleted more dye was added from the stock bottle. The alcohol bottle likewise was replenished frequently from a larger stock bottle.

It would be a simple matter to harbor the viable virus of serum hepatitis both in the dye container and in the alcohol bottle for a long period of time under these favorable conditions. The tattooer stated that his work was not satisfactory unless he "drew blood" with the needles. Blood and serum were therefore directly introduced into the dye containers, and it would seem possible that one customer who was a carrier could contaminate all dye containers and the alcohol container as well. That this is possible is further supported by the small amount of serum necessary to transfer the virus, 0.001 cc. according to Scheinburg.[10] Sawyer and others[11] have suggested that as high as 6 per cent of the population are periodic carriers. They based their results on tracing the infected donors in pooled plasma.

CONTROL MEASURES

Certain control measures were put into effect after the preliminary report of suspected tattoo-spread hepatitis in Panama City and Colon. On Feb. 8, 1950 all tattoo operations were ordered suspended until the tattooists could be instructed in a safe way to operate. More acceptable technic was explained to the three operators on the Pacific side and the one on the Atlantic side. Two of the establishments reopened on the Pacific side and one on the Atlantic side, with the following modus operandi. Individual containers of dye are used for each customer. These are boiled for at least 30 minutes before reuse. Dye for each case is transferred from central containers to an individual container with a tongue depressor, which is used only once. Each needle is boiled for 30 minutes before reuse. One needle battery is used instead of the four which were used previously. This technic would seem adequate, provided it is religiously followed, to prevent the transfer of serum from one customer to another.

CONCLUSIONS AND SUMMARY

1. Serum hepatitis and infectious hepatitis remain entities by virtue of differences in their epidemiology and incubation period.

2. Twenty-six cases of hepatitis were analyzed for a possible common source of infection. Eighteen (69 per cent) of the patients were found to have been tattooed in Panama City within 49 to 154 days prior to the onset of their symptoms. Seventeen of these 18 men had been tattooed at one place. This incubation period is compatible with the incubation period of serum hepatitis.

3. Among routine hospital admissions in a series of 200 patients, 30 per cent were found to have been tattooed, but only 8 per cent were tattooed in Panama City (comparing identicals) and none of these were tattooed within the incubation period of serum hepatitis. Among the 26 hepatitis patients, 88 per cent had been tattooed in Panama City and 69 per cent within the incubation period of serum hepatitis. The possibility is offered that tattooing is an important mode of transmission of hepatitis among service personnel. 4. The tattooing technics were investigated and found to be such that viable virus of serum hepatitis could be transferred from one customer to the next. Corrected technics, if adhered to, should prevent tattoo-needle inoculation.

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ADVANCES IN THE MANAGEMENT OF JAUNDICE

Experiences with 500 Jaundiced Patients

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The jaundiced patient presents a peculiar problem for treatment inasmuch as the icterus itself, although only a symptom of some underlying disease, produces certain physiological disturbances which have to be considered in the treatment of the patient. Moreover, regardless of the underlying condition causing the jaundice, which must be kept in mind during the planning of the treatment, the factor of liver changes must be considered in the adequate care of the icteric patient. It is presently acknowledged that whether the jaundice is due to a hepatitis (virus or toxic) or whether it is due to some disease process in the extrahepatic biliary tract, there is an impairment of the liver parenchyma. The damage, however, is of variable degree. Severe icterus brings with it a number of changes within the liver itself and within the digestive tract, which must be appreciated when therapy is planned. In treating patients with jaundice one must follow a definite plan which should include all the various factors that directly or indirectly may affect the various functions of the hepatobiliary tract.

In general, the treatment of jaundice has for its objective the removal or destruction of the causative factor, the amelioration of symptoms, the prevention of further damage and the repair of already damaged tissues at the earliest time and by the simplest mode, in order to prevent profound changes which may lead to scars and severe impairment of function.

The above objectives have been considered in the therapeutic regimen of over 500 jaundiced patients during the past five years. These patients included all types of jaundice and presented variable degrees of liver damage. The youngest patient was 10 years

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of age and the oldest 76. The group was composed of both white and Negro, male and female patients. Some of these were seen during the acute (first) attack of jaundice and some during recurrent episodes. After discharge from the hospital many of them were followed in the outpatient clinic so that their later course could be observed.

This paper is based on the experiences gained from the therapeutic results in the above group of patients. In it are presented the various therapeutic procedures employed in this group. It should be stressed that not all the procedures were applicable in all patients and that some procedures have been used only on an exceedingly limited scale because they were only recently added to the therapeutic armamentarium. With these exceptions in mind, the following therapeutic plan is presented and some of the underlying basic principles are discussed.

REST

Regardless of the type of jaundice, it is advisable that the icteric patient be put to bed and kept there until the course of the disease or the etiologic basis is well established. Some types of jaundice (for example, those due to liver damage, particularly of the virus nature) are extremely sensitive to physical exertion.[1] Hence, bed rest as complete as possible in given circumstances should be instituted. Bed rest prevents jarring and massage of the liver, and it may also prevent the excessive metabolism of other tissues which usually occurs during exercise. Some of the products of excessive metabolism, if not toxic to the liver per se, have to be detoxified by the liver, thus increasing the work of a damaged organ and possibly resulting in greater impairment. There is sufficient available evidence to support the need for strict bed rest particularly during the acute and convalescent phases of hepatitic icterus.

DIET

Since in most instances there is as yet no specific treatment for liver disease, and since it has been found that certain dietary substances are important in the production or in the prevention of liver damage,[2] it is obvious that the diet is of utmost importance in patients with jaundice. Nevertheless there are certain controversial points concerning the dietary management of such patients. Essentially there is agreement that all patients with jaundice should have a high caloric, high vitamin, high carbohydrate and high protein diet.

Fats.—The amount of fat in the diet is somewhat controversial. Some believe that the fat content should be low,[3] others that it should be average [4] and some that it should be high [5] in order to give the patient a high caloric, palatable diet. My observations indicate that in patients with acute jaundice the fat content plays a comparatively minor role and that it is immaterial whether the fat content is average, slightly above or slightly below the average. I like to give these patients a high caloric diet so prepared that they consume it all. If a little more fat will make the diet more palatable there is no objection to giving more fat. In patients with the chronic type of jaundice (particularly cirrhosis) I believe that the amount of fat should be small (average or less than average) because in these patients less fat is better handled from the point of view of both absorption and transportation. Fats of animal origin (excluding dairy fats) with their high content of unsaturated fatty acids are particularly injurious, increasingly so after heating.[6]

Fats are necessary for building up a high caloric diet. Second, diets without fats are not palatable and are poorly taken. Third, fats contain all the fat-soluble vitamins which are also necessary in body metabolism.

Because of these factors a certain amount of fat is a necessary constituent of any diet which has to be used for any length of time. The amount of fats ingested, however, must be regulated in certain patients with jaundice. Small quantities of fats should be given to those who have either poor digestion or poor absorption of fats as evidenced by steatorrhea or in whom the turnover of fat is pathologic and in whom the intake of even average amounts of fat may lead to increased fat deposits in the liver. Since it is agreed that a fatty liver is a "sick" liver, one which is more susceptible to injury from endogenous and exogenous hepatotoxins,[7] it is apparent that in order to protect the liver one should prevent excess deposition of fat in it. Obviously in the acute stages of jaundice which last for a short time the degree of fat absorption and fat retention plays a minor role. In the patients with chronic jaundice, however, in whom there is danger of increasing the already pathologic fat stores in the liver, the amount of fat may have to be curtailed, sometimes drastically.

Carbohydrates.—For many years diets high in carbohydrates have been advocated for patients with jaundice. This has continued until the present day. Patients with jaundice do require a carbohydrate intake anywhere from 350 to 500 Gm. daily, depending on the size of the person. If this amount of carbohydrate cannot be given by mouth, part of it may have to be given by a parenteral route. It is important to watch for glycosuria in order to be able to control it if it should occur. This control can take the form of more frequent feedings with smaller amounts of carbohydrates or in rare instances the administration of small doses of insulin to help in the metabolism of the ingested carbohydrate. The carbohydrates which are easily digested and of low residue are preferable for jaundiced patients.

Proteins.—Not until the late 1930's was the importance of proteins in jaundice recognized. Prior to that era a diet low in protein was the treatment of choice for such patients. In the past decade, however, a diet high in protein of high "biologic value" has become

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the accepted treatment for jaundiced patients, not only because proteins are needed for rebuilding damaged tissues but also because they contain many amino acids which are essential for normal metabolism of the liver. The value of the various individual amino acids for certain specific metabolic functions of the body is continuously being recognized. Furthermore, the products of some of these proteins are of great importance for the normal function of endocrine and exocrine glands, the secretions of which in turn influence liver metabolism. The experiences with nutritional deficiencies of some prisoners of war during World War II have demonstrated the significant changes that may occur in the body economy, such as body fluid, hormonal secretions and immunity, from an insufficient supply of protein. Proteins are greatly needed not only by patients with liver disease but also by those with jaundice of extrahepatic origin who have to undergo surgical intervention, because hypoproteinemia interferes with prompt and adequate wound healing.

VITAMIN SUPPLEMENTS

Patients with jaundice should receive additional vitamin supplements despite a diet which is high in calories and vitamins. Usually additions of all vitamins are necessary.

Fat-Soluble Vitamins.—Vitamin A: It has been shown that the plasma of acutely jaundiced patients contains little vitamin A even though the liver may have large quantities of it. In chronically jaundiced patients, however, stores of vitamin A in the liver are much smaller than in patients with acute hepatitis or with extrahepatic biliary tract involvement.[8]

The low plasma vitamin A level in acute cases of jaundice seems to be due to failure of the liver vitamin A to reach the circulation. Thus in patients with hepatitis there is less rise of the vitamin A level in the plasma after a given dose of vitamin A than in nonjaundiced persons.[9] Large amounts of vitamin A given orally may increase the plasma vitamin A level by first saturating the liver parenchyma and then causing an overflow of vitamin A into the plasma. These observations suggest that patients with jaundice require large supplements of vitamin A. Doses of 50,000 to 100,000 units of vitamin A in oil are most likely to cause a rise of the plasma vitamin A level. The recent preparation of vitamin A in aqueous solution is better absorbed and more economical because a dose about half the unit value of the oily solution will raise the vitamin A level of the plasma to a similar height.[10] The vitamin A supplement should not be given in the form of cod liver oil, because the fatty acids in the latter might be injurious to the liver.[11] In patients who cannot take anything orally, vitamin A can be given parenterally, preferably in the form of vitamin A palmitate in aqueous dispersion.[12]

Vitamin D and Vitamin E: At present there seems to be no apparent need for or gain from additional amounts of vitamin D. In the experimental animal vitamin E prevents liver necrosis, and doses of 100 to 300 mg. of tocopherol daily have been suggested for hepatic injury in man.[13]

Vitamin K: Lack of vitamin K is manifested by characteristic symptoms. The need for this vitamin and the amount to be used in various types of jaundice is usually determined by the plasma prothrombin level. A good and prompt rise of the prothrombin level after the intake of vitamin K is frequently considered a sign of good liver function.

Water-Soluble Vitamins.—Vitamin C (Ascorbic Acid): Vitamin C, which is stored in only small amounts in the body, is depleted rapidly; therefore patients with jaundice should be given large doses of this vitamin (500 to 1,000 mg. a day) because it influences favorably carbohydrate and protein metabolism and prevents fat deposition.

Vitamin B Complex: The vitamins of the B complex group are possibly even more important for the jaundiced patient than the vitamins previously mentioned. This holds true particularly for the so-called unknown factors; therefore it is advisable to give jaundiced patients large supplements of natural vitamin B complex rather than only individual B complex fractions which are at present prepared synthetically. Although the need for thiamine hydrochloride, riboflavin, nicotinic acid and pyridoxine is indisputable, certain other biological substances, some of which are at present still unnamed, seem to have much greater influence than the aforementioned fractions. Moreover, it is not advisable to give large doses of the components of the B complex since unbalanced doses may produce liver injury. In the treatment of the jaundiced patient it is preferable to use crude liver extract, liver powder or yeast powder (or tablets) rather than the synthetic preparations. The recent experiences with folic acid and particularly with vitamin B_{12}[14] in liver disease are examples of the importance of the natural B complex preparations, because they show that some of the benefits which were obtained previously with liver extract, liver powder or yeast powder were probably, to some degree, due to the above two substances which are part of the B complex group. Vitamin B_{12} should be given in large doses (30 micrograms daily or more) to patients with liver disease.

MISCELLANEOUS DIETARY FACTORS

In planning a diet for a jaundiced patient one must consider not only the three main foodstuffs, carbohydrates, proteins and fats, but the various accessories. The average patient with liver disease should get a diet which is low in salt, particularly sodium. It is necessary to cut down the salt intake because in jaundice, particularly that due to liver disease, there is definite sodium retention,[15] which may in later stages lead to water retention, edema and finally ascites.

The quantity and quality of the diet are not the only factors to be considered in planning the dietary regimen of the jaundiced patient. One should realize that many of these patients have anorexia, nausea and/or vomiting. Hence the number of feedings, size of each feeding and its particular composition are important. It is at times

8. Popper, H., and Steigmann, F.: Clinical Significance of Plasma Vitamin A Level, J. A. M. A. **123**: 1108 (Dec. 25) 1943.
9. Popper, H.; Steigmann, F., and Zevin, S.: On the Variations of the Plasma Vitamin A Level After the Administration of Large Doses of Vitamin A in Liver Disease, J. Clin. Investigation **22**: 775, 1943.
10. Popper, H.; Steigmann, F., and Dyniewicz, H.: The Influence of Antioxidative and Dispersing Agents on Vitamin A Absorption: Therapeutic Implication in Endogenous Hypovitaminemia A, Gastroenterology **10**: 987, 1948.
11. György, P.: Massive Liver Necrosis, in the Conference on Liver Injury, 1949, Transactions of the Eighth Conference, New York, Josiah Macy, Jr. Foundation, 1950, p. 37.
12. Unpublished data.
13. György, P.: Relation of Dietary Factors to Liver Injury, in the Conference on Liver Injury, 1947. Transactions of the Sixth Conference, New York, Josiah Macy, Jr. Foundation, 1948, p. 67.
14. Popper, H.; Koch-Weser, D., and Szanto, P. B.: Protective Effect of Vitamin B_{12} upon Hepatic Injury Produced by Carbon Tetrachloride, Proc. Soc. Exper. Biol. & Med. **71**: 688, 1949.
15. Farnsworth, E. B.: Electrolyte Partition in Patients with Edema of Various Origins: Sodium and Chloride, Am. J. Med. **4**: 338, 1948.

preferable to serve small meals at frequent intervals in order to permit the patient to eat small amounts slowly rather than to offer him a large meal which will make him feel bloated, nauseated and anorexic for the remainder of the day. The patient who experiences such discomfort after eating one meal is not going to enjoy the thought of eating another meal. The daily food requirements should therefore be offered at frequent intervals in small portions and at appropriate times. When proteins are given as supplemental protein drinks, whether as hydrolysates[16] or casein mixtures,[17] they should be given after meals rather than shortly before a meal. The food should be prepared and served in as pleasant a way as possible, because many patients eat not only with their mouths but also with their "eyes and nose."

Parenteral Solutions.—If a patient is not able to take all his caloric requirements by mouth some arrangements for parenteral supplements must be made, the latter consisting of dextrose and/or amino acid solutions. Dextrose, however, is at times given intravenously for other reasons, circulatory and metabolic.[18] If parenteral fluids are needed they should be given judiciously and at the correct time. To give parenteral fluids to a patient before the larger meals will result in a decreased appetite and a lack of enthusiasm for that particular meal. If protein hydrolysates are given parenterally because the patient cannot ingest sufficient proteins otherwise, these fluids definitely should be given after the last meal. The parenteral injection of protein hydrolysates gives the patient in some instances a sensation of satiety and, particularly when given too fast, may actually lead to nausea with or without vomiting.

The dietary therapy should be so arranged that it does not interfere with other necessary therapeutic or diagnostic procedures. Since most jaundiced patients —in this series—seem to eat best in the morning, it is advisable to plan a good breakfast for them with somewhat smaller meals during the remainder of the day. Furthermore, necessary injections of crude liver, vitamins and antibiotics which are part of the therapeutic regimen should be given in the morning before a meal or long enough after a meal so that the patient will not be upset too shortly before or after mealtime.

MEDICINAL SUPPLEMENTS

Calcium.—In some patients with jaundice, particularly in those with severe hepatitis associated with toxemia, calcium should be given in various doses (10 to 20 cc. of a 10 per cent calcium gluconate solution) and at various intervals during the day. Calcium appears to neutralize[19] some hepatotoxins (guanidine and related compounds) which accumulate in the blood stream of patients severely ill with liver disease.

Antibiotics.—Penicillin and streptomycin are frequently indicated for treatment of infections associated with jaundice, regardless of how mild the infections may appear to be. These antibiotics are helpful especially in treatment of the surgical types of jaundice. In cases of hepatitis (virus type) aureomycin has given some striking results particularly in cases of hepatic coma as observed by others[20] and by me in this series. I did not have sufficient experience with chloramphenicol (chloromycetin®) for any comment as to its efficacy in cases of hepatitis.

Sedatives.—For sedation, paraldehyde, chloral hydrate and slow acting barbiturates are safest for icteric patients. Use of opiates is contraindicated unless absolutely necessary. Meperidine (demerol®) hydrochloride may be used as a narcotic. Salicylates are well tolerated and can be given freely as analgesics.

Laxatives.—Many icteric patients suffer from constipation. In them a mild saline laxative is indicated.

Digestants.—For patients whose illness is more chronic and who complain of flatulence, belching and abdominal discomfort, the judicious use of dilute hydrochloric acid, bile salts and/or pancreatic substance has proved helpful.

Antipruritics.—Pruritus is encountered mostly in cases of surgical jaundice and is frequently one of the complaints with which it is most difficult to deal. Acetylsalicylic acid and ergotamine tartrate have been of little help. The antihistaminics have not proved too efficacious in treatment of my patients. Procaine hydrochloride in a 0.1 to 0.2 per cent solution (1 to 2 Gm. of procaine hydrochloride in 1,000 cc. of 5 per cent dextrose solution) has offered striking relief to some patients with pruritus.

Diuretics and Diuretic-like Substances.—In some patients treatment with mercurial diuretics alone may give results; in others ammonium chloride and mercurials are better. In some cases the addition of hypertonic dextrose solution or dehydrocholic acid (decholin®) (10 cc. of 10 per cent solution) increases the diuretic effect. Mercurials should be used cautiously.

Testosterone.—The injection of testosterone has been of aid in a small group of patients with cirrhosis. The basis for use of this substance is theoretical, but clinical evidence has accumulated to indicate that a trial of it is worth while.[21] It is possible that testosterone aids in getting rid of ascites by acting against the excess of estrogenic substances which the liver is unable to destroy and perhaps more so by its anabolic character.[22]

Crude Liver.—Injections of crude liver are beneficial because they frequently improve the appetite of the patient and at times appear to promote diuresis by supposedly counteracting the antidiuretic principle found in patients with hepatic jaundice.

Salt Substitutes.—The administration of one of the saltlike substances may be helpful because it will aid the patient in following a diet low in sodium.

Condiments and Spices.—Use of pepper, salt, mustard and other similar substances is best avoided.

Fluids.—The fluid intake should be moderately restricted to around 1,500 cc. More severe restriction may lead to complaints by the patient.

Lipotropic Substances.—In the past few years much has been written about the so-called lipotropic substances which supposedly help fat transport in the

16. Such as ledinac® (containing liver protein digest 54 per cent and maltose 38.5 per cent with vitamins) or lonalac® a powdered whole milk preparation of low sodium content.

17. Such as casec,® a milk protein preparation, and meritene,® a whole protein supplement fortified with vitamins and minerals.

18. Wakim, K. G.: Effect of Certain Substances on Intrahepatic Circulation of Blood in Intact Animal, Am. Heart J. **27**: 289, 1944. Soskin, S., and Hyman, M.: Physiologic Basis of Intravenous Dextrose Therapy for Diseases of Liver, Arch. Int. Med. **64**: 1265 (Dec.) 1939.

19. Minot, A. S.: Mechanism of Hypoglycemia Produced by Guanidine and Carbon Tetrachloride Poisoning and Its Relief by Calcium Medication, J. Pharmacol. & Exper. Therap. **43**: 295, 1931. Cutler, J. T.: Influence of Diet on Carbon Tetrachloride Intoxication in Dogs, ibid. **45**: 209, 1932. Cantarow, A.; Stewart, H. L., and Morgan, D. R.: Experimental Carbon Tetrachloride Poisoning in Cat: Influence of Calcium Administration, ibid. **63**: 153, 1938.

20. Sborov, V.: Personal communication to the authors.

21. Rosenak, B. D.; Moser, R. H., and Kilgore, B.: Treatment of Cirrhosis of the Liver with Testosterone Propionate, Gastroenterology **9**: 695, 1947.

22. Kinsell, L. A.: Factors Affecting Protein Balance in the Presence of Chronic Viral Liver Damage, Gastroenterology **11**: 672, 1948.

body.[23] At present a number of individual lipotropic substances (methionine,[24] choline and inositol) mixtures of lipotropic substances and liver,[25] powdered liver [26] and gastric mucosa are available for therapeutic use. Studies by various workers have shown that these substances have therapeutic value in carefully selected patients with cirrhosis of the liver on a nutritional basis or in patients with fatty livers.[27] The results of lipotropic therapy in patients with acute or chronic hepatitis on a virus basis have been disappointing.[28] In acute hepatitis characterized by severe toxic fatty changes, such as those following the injection of carbon tetrachloride or other hepatotoxic drugs, the administration of lipotropic substances may be of some value.[29] In general it may be stated that lipotropic substances appear to be of therapeutic value mainly in those patients in whom excessive fatty deposits in the liver are prominent features.

Alcohol.—Use of alcoholic beverages is prohibited for patients with jaundice. They are detrimental to patients with chronic hepatitis (on a deficiency basis) and may be harmful even to those with the virus form.[30]

PROCEDURES FOR TREATMENT OF SPECIAL CONDITIONS IN THE JAUNDICED PATIENTS

Acute Hepatic Coma.—In cases of severe hepatic insufficiency (fulminant hepatitis or actual hepatic coma) large amounts of dextrose must be given intravenously. Occasionally in these patients continuous infusion of 5 to 10 per cent dextrose solution is necessary. In some patients the additional use of sixth-molar sodium lactate solution is of value. The dextrose solution should be reinforced with large doses of ascorbic acid, thiamine hydrochloride 100 to 200 mg., riboflavin and niacin (nicotinic acid) or nicotinamide.[31] Vitamin B complex in the form of crude liver extract should be given daily and in large doses (3 to 5 cc.). Methionine given intravenously is occasionally helpful. Intravenous administration of liver in the form of a concentrate (intraheptol®) gave striking results in a few instances of hepatic insufficiency. Vitamin K should be given in doses large enough to keep the prothrombin level at normal range. If these patients have much fluid, edema, anasarca and ascites, a 25 to 50 per cent dextrose solution can be given intravenously at slow drip as part of the carbohydrate quota and the remainder as a 5 or 10 per cent solution. Although there may be sodium retention one must be careful to check for the possibility of hypochloremia which may occur if these patients are kept for a long time on a salt-free diet. In hepatic insufficiency the administration of oxygen in high concentration by tent, mask or tube occasionally has seemed to be of great value. In some of these patients transfusions of fresh whole blood are of value because they combat both anemia and prothrombin deficiency. Sometimes plasma may be used in addition to fresh whole blood; the plasma however should be freshly prepared rather than a multidonor mixture. If the latter, it should have been irradiated with ultraviolet rays to prevent the possibility of homologous serum jaundice in the future.[32]

Extrahepatic Obstruction.—Most patients who are jaundiced as the result of an extrahepatic factor have to undergo surgical intervention for relief of the obstruction. Adequate liver therapy before operation will make these patients better surgical risks and will result in a better course during the operation and postoperatively. In these patients particular attention must be given to the prothrombin bleeding and coagulation time, to the fluid and electrolyte balance and to the type of anesthesia they will receive. The prevention of anoxia of the liver—by giving the patient oxygen and keeping the blood pressure at an adequate level—during the operation is important in these cases.

Once surgical intervention is deemed necessary it should be performed at the optimal time. In face of a dropping icterus and otherwise good condition of the patient, the operation may be postponed. However, in face of an extrahepatic obstruction with rising icterus, rising nonprotein nitrogen, falling hippuric acid synthesis and lowered cholesterol esters, surgical intervention should be prompt.

Jaundiced patients who are being prepared for surgical intervention should receive some type of antibiotic therapy. In most instances penicillin is sufficient; in some, however, depending on the associated infection, streptomycin, aureomycin or chloramphenicol may also be administered.

Fibrosis (Mesenchymal Reaction).—The presence of fibrosis in the liver in patients with chronic jaundice is usually manifested by additional signs, such as ascites, edema, distended veins in the abdominal wall, esophageal varices and splenomegaly. In these patients a stricter regimen of salt-free diet, diuretics and administration of vitamin B complex factors is necessary. Salt-free serum albumin is useful in some patients.[33] In addition, some patients may require abdominal paracentesis. Experiences with pituitary adrenocorticotropic hormone (ACTH) in such patients are still too limited to permit comment on the efficacy of the agent.

Infection.—In a jaundiced patient the presence of an infectious process, whether part of the underlying disease state or whether secondarily superimposed, adds to the hazards of the case. Infection should be combated by one or more of the antibiotics and by more intensive liver therapy in general.[34]

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23. Best, C. H.; Hershey, J. M., and Huntsman, M. E.: The Control of the Deposition of Liver Fat, Am. J. Physiol. **101**: 7, 1932. Best, C. H., and Huntsman, M. E.: The Effects of the Components of Lecithin upon Deposition of Fat in the Liver, J. Physiol. **75**: 405, 1932.
24. Mconine,® a synthetic racemic methionine supplied by Wyeth, Inc.
25. Methiochol,® supplied by U. S. Vitamin Corporation.
26. Jayron, supplied by Viobin Corporation, is desiccated and defatted mammalian liver; 1 pound is equal to 4 pounds of whole liver.
27. Russakoff, A. H., and Blumberg, H.: Choline as an Adjuvant to the Dietary Therapy of Cirrhosis of the Liver, Ann. Int. Med. **21**: 848, 1944. Broun, G. O., and Muether, R. O.: Treatment of Hepatic Cirrhosis with Choline Chloride and Diet Low in Fat and Cholesterol, J. A. M. A. **118**: 1403 (April 18) 1942. Rimmerman, A. B.; Schwartz, S. O.; Popper, H., and Steigmann, F.: Dietary Factors in the Treatment of Cirrhosis Without Jaundice, Am. J. Digest. Dis. **11**: 401, 1944. Morrison, L. M.: The Response of Cirrhosis of the Liver to an Intensive Combined Therapy, Ann. Int. Med. **24**: 465, 1946. Barker, W. H.: The Modern Treatment of Cirrhosis of the Liver, M. Clin. North America **29**: 273, 1945. Labby, D. H.; Shank, R. E.; Kunkel, H. G., and Hoagland, C. L.: Cirrhosis of Liver, J. A. M. A. **133**: 1181 (April 19) 1947. Beams, A. J.: Treatment of Cirrhosis of Liver with Choline and Cystine, ibid. **130**: 190 (Jan. 26) 1946. Steigmann, F.: Efficacy of Lipotropic Substances in Treatment of Cirrhosis of Liver, ibid. **137**: 239 (May 15) 1948.
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30. Damodaran, K., and Hartfall, S. J.: Infective Hepatitis in the Garrison of Malta, Brit. M. J. **2**: 587, 1944.
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33. Watson, C. J., and Greenberg, A.: Certain Effects of Salt Poor Human Albumin in Cases of Hepatic Disease, Am. J. Med. Sc. **217**: 651, 1949.
34. Markowitz, J.; Rappoport, A., and Scott, A. C.: Prevention of Liver Necrosis Following Ligation of Hepatic Artery, Proc. Soc. Exper. Biol. & Med. **70**: 305, 1949.

Hemolysis.—Some jaundiced patients have associated hemolytic phenomena. In these the factors causing hemolysis should be identified and removed if possible. Blood transfusions should be given as often as necessary to prevent anemia with the associated anoxia of the liver.

Convalescent Period.—Patients who are convalescing from jaundice, particularly those who are recovering from hepatitis, should only gradually return to their previous diet and activities. Many of these patients have to restrict the intake of fatty foods and alcoholic beverages. They should be careful to avoid exposure to excessive strain, infection or other influences which may decrease their resistance and lead to possible recurrence of the hepatitis. Patients with cirrhosis must watch their diet and abstain from alcohol indefinitely.

CONCLUSION

All jaundiced patients, whether they have hepatitis or extrabiliary tract conditions, have a certain degree of liver damage and should therefore be treated with an intensive liver regimen. Various steps in the present management of jaundice have been presented, and the basis for some of them has been discussed. All jaundiced patients, particularly before the exact nature of the jaundice is known, deserve the most intensive liver therapy in order to prevent some of the dire complications which may result from improper management of such cases.

Mortality Percentage of Patients with Medical Jaundice During Initial Hospital Admission

Types	1939-1944	1945-1950*
All jaundice cases	38.2	25.1
Infectious hepatitis	6.5	5.1
Toxic hepatitis	25.0	16.8
Cirrhosis with jaundice	63.0	38.8
Cirrhosis without jaundice	31.0	17.8
All cirrhosis cases	48.0	32.0 15.6†

* Patients treated through the month of May, 1950.
† If treated with lipotropic substances in addition.

The results of such a regimen as that presented above can best be gleaned from the accompanying table, which shows the immediate mortality of patients with medical jaundice before and after institution of the newer therapy.

30 North Michigan Avenue.

ABSTRACT OF DISCUSSION

DR. T. L. ALTHAUSEN, San Francisco: Dr. Steigmann's summary of the modern management of jaundice is excellent. There are some areas of disagreement in our handling of patients, but these are few. I would like to point out the necessity of giving supplemental vitamin D. Dr. Steigmann recognizes the importance of calcium metabolism in jaundice, because he advised the administration of salts of calcium. Supplemental amounts of vitamin D are also necessary because calcium even in large amounts is not absorbed well when there are excessive amounts of fat in the intestinal tract, whereas supplemental amounts of vitamin D will provide for more nearly normal absorption of calcium. With a few exceptions administration of bile salts is contraindicated in most diseases of the liver because bile salts stimulate the liver to secrete bile, and it does not seem therapeutically correct to stimulate a sick organ to greater activity, whether that organ be a sick heart or a sick liver. For this reason I believe that as a rule bile salts should not be administered to patients with jaundice. The third point is related to low salt diets, which are in most cases beneficial to patients with diseases of the liver. However, there is a certain amount of danger in overdoing a good thing, particularly if the patient has ascites and is being tapped. I saw at least two patients who were in a semicomatose condition after a prolonged period on a low salt diet and after removal of ascitic fluid but who regained consciousness immediately after the administration of sodium chloride. Stimulated by this experience, I determined the amount of sodium actually lost during a paracentesis and found that it may amount to as much as 15 Gm. I want to commend Dr. Steigmann on his discussion of the importance of judiciously timing the intravenous feedings. Such feedings definitely impair the patients' appetite when given shortly before a meal. This fact has never been emphasized sufficiently in the literature.

DR. FREDERICK STEIGMANN, Chicago: Only in chronic cases of jaundice do I suggest administration of bile salts. As Dr. Althausen mentioned, patients with acute jaundice are not given bile salts because it is not desirable to stimulate a sick organ. In some instances I, too, have noticed that if the low salt diet is followed by the patient without careful observation by the physician, the patient may become hypochloremic.

ELECTROENCEPHALOGRAPHICALLY CONTROLLED ANESTHESIA IN ABDOMINAL SURGERY

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The primary objective of the surgeon is to lower mortality and morbidity rates. For this reason he is always interested in developments that give promise of attaining this end. In the flush of enthusiasm about some new product or device the tendency is to think in terms of panaceas rather than to maintain a calm point of view and evaluate its true place in one's armamentarium. It is too early to classify the subject of this presentation, electroencephalographically controlled anesthesia in abdominal surgery. There is no field in medicine that the surgeon has followed with more interest and no specialty on which he has been more dependent than anesthesiology. Due credit must go to those physicians in active practice, physiologists and others in related basic science fields and those connected with pharmaceutical organizations, whose collective contributions since use of the first crude anesthetic agent have brought anesthesia to the present high plane of perfection.

Surgical anesthesia may be defined as the induced loss of sensation of a part, or of the body as a whole, with sufficient mental and muscular relaxation of the patient to permit optimal surgical technic for the operative procedure necessary. Short of this state, the patient has not arrived at a state of surgical anesthesia. Anesthetic agents vary because of their particular physical and chemical properties. One of the properties they have in common, however, is their ability to diminish and finally to produce loss of irritability and conductivity of nerve tissue when applied in adequate concentration. In general anesthesia, with certain aspects of which this paper is concerned, the agent or agents employed reach the nervous system by way of the blood stream. During the process of increasing the concentration of the anesthetic agent in the tissue, progressive inhibition of the normal function in the individual components of the nervous system is manifested by certain

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From the Division of Surgery (Dr. Mayo), the Laboratory of Electroencephalography, Section of Physiology (Dr. Bickford) and the Section on Anesthesiology (Dr. Faulconer) of Mayo Clinic.

reflex changes and alterations in spontaneous motor activity. From these changes the trained observer is able to make a fair estimate of the depth of anesthesia. On a basis of this estimate and his past experience he finds it possible in most cases to induce and maintain optimal conditions for the surgical procedure contemplated. The diagnosis of depth of anesthesia in this manner has never been an exact science but is truly an art.

In the hope that electroencephalographic changes occurring during surgical anesthesia might provide a basis for a more objective and exact estimate of the depth of anesthesia a critical study of these changes was made.[1] The investigation was confined primarily to persons undergoing operations in which nitrous oxide-oxygen-ether anesthesia was used. As an outcome of this work it was seen that there were changes in the electroencephalographic pattern of sufficient clarity, magnitude and consistency to allow these changes to be related to depths of anesthesia progressing from loss of consciousness to complete respiratory paralysis. These changes in pattern arranged in order of increasing depth of anesthesia seemed to fall naturally into seven levels.[1] The levels are indicated in figure 1.

A study of the characteristics of the patterns occurring with increasing depth of anesthesia revealed the important fact that the total output of electrical energy per unit of time represented by the height and the duration of the brain waves was maximum in every case at a time closely approximating the lightest level of surgical anesthesia. As anesthesia became deeper there was a consistent and progressive drop in the total output of energy represented by the brain waves until at a level coinciding with respiratory paralysis this output of energy was, for practical purposes, zero.

The constancy of the relationship between the output of electrical energy measured at the scalp and the depth of anesthesia suggested to one of us (R. G. B.) the possibility of utilizing the brain potentials to regulate automatically the administration of certain anesthetic agents. To accomplish this an electronic integrator was added to the electroencephalograph. This served the purpose of storing the energy output until it had reached a certain predetermined amount, whereupon

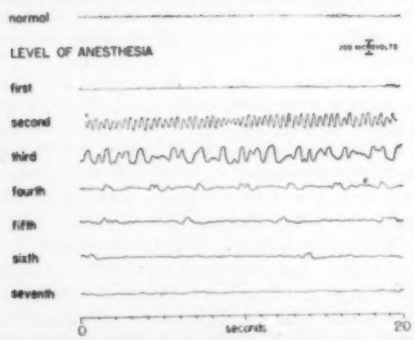

Fig. 1. — Electroencephalographic levels of anesthesia (nitrous oxide-oxygen-ether).

the stored energy was instantly released and the storage process begun anew. Thus, with an exceedingly active brain-wave pattern this cycle would be repeated with a much greater frequency than with an inactive brain-wave pattern.

1. Courtin, R. F.; Bickford, R. G., and Faulconer, A., Jr.: Classification and Significance of Electro-Encephalographic Patterns Produced by Nitrous Oxide-Ether Anesthesia During Surgical Operations, Proc. Staff Meet., Mayo Clin. **25**: 197-206 (April 12) 1950.

Now it became possible to utilize the energy discharge at the termination of each of the cycles just described to "trigger" a relay circuit activating a pump. A pumping system was designed so that each energy discharge would cause the propulsion of a fixed amount of anesthetic agent into a vein or an ether vaporizer. In this manner a system was established which would

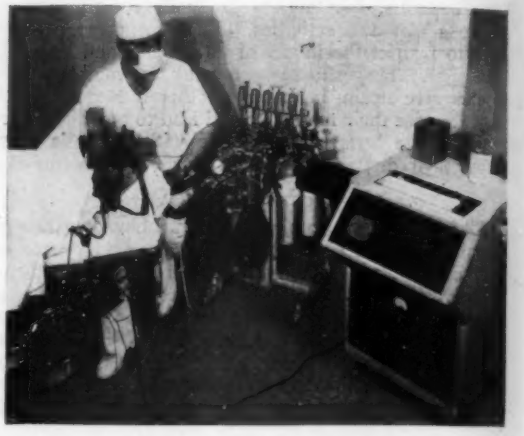

Fig. 2.—Automatic administration of ether.

administer the anesthetic agent (ether or thiopental [pentothal®] sodium) through the desired channels at a rapid rate when the brain-wave pattern revealed great activity and at a slower rate when the pattern revealed less activity.

Application of this device to the administration of thiopental sodium and ether to rabbits, cats and monkeys established the fact that a desired level of surgical anesthesia could be maintained automatically for long periods of time (two to three days) without human interference. The depth of anesthesia thus maintained could be established by suitable adjustment of the integrating mechanism. Experience demonstrated that this automatic system tends to compensate for factors which disturb equilibrium. For example, should there be a leak in the intravenous or inhalation channel or should the anesthetic agent be added by another means, the rate of administration governed by the system makes an appropriate compensation as soon as the disturbing factor is reflected in alteration of the brain-wave pattern.

The idea of the automatic electroencephalographic control of anesthesia was developed by one of us (R. G. B.)[2] and co-workers, in collaboration with Drs. Faulconer, Courtin and Soltero and Miss Haefliger. Another of us (C. W. M.) became interested in it while it was still in the state of animal research, and he was privileged later to participate as a surgeon in the practical application of the system to man. To date it has been used in performing major surgical procedures on more than 50 adult patients of varying ages and of both sexes without untoward effect (fig. 2). The electroencephalogram foretells a change in depth of anesthesia many seconds before the change is apparent to an anesthetist. It instantly and automatically adjusts the administration of the agent to compensate for a change in depth. Thus it is more capable than the

2. Bickford, R. G.: Automatic Electroencephalographic Control of General Anesthesia, Electroencephalog. & Clin. Neurophysiol. **2**: 93-96 (Feb.) 1950.

anesthetist of maintaining a constant level. If the surgeon will wait for the establishment of the necessary level of surgical anesthesia before opening the peritoneal cavity and, again after abdominal exploration, before starting the technical accomplishment of the main surgical procedure, the uninterrupted relaxation obtained by this automatic administration of anesthetic agents is most gratifying. However, the use of this method of anesthesia does not eliminate the need for the well trained anesthetist.

In addition to the practical potentialities of electroencephalographically controlled anesthesia related directly to clinical surgery, electroencephalography has opened a new door to research in the field of anesthesiology. Automatic anesthesia may even have a therapeutic value in certain neuropsychiatric conditions or physical states in which a constant degree of controlled rest and relaxation may be desirable. For the investigator who must depend on anesthetized animals for his studies this method offers for the first time precise control and objective evidence of the depth of anesthesia—an important consideration in the evaluation of the results of many investigations.

Continuing efforts in this particular field of experiment and study give promise of simplification and development of the apparatus to a state of compactness and reliability which will add much to the safety of administration of certain anesthetic agents and make the method more generally available to research projects. It seems to have great practical potentiality.

ABSTRACT OF DISCUSSION

DR. ALBERT FAULCONER JR., Rochester, Minn.: It is not our purpose to propose the substitution of a rather complex machine for a competent anesthetist. We wish to make that very clear. We do feel that there are certain applications, immediate and potential, which can be made with this device, and they can be classified for convenience under four major headings: First, this device may find a field of usefulness in clinical anesthesia when applied in circumstances in which the prolonged maintenance of an even level of anesthesia is desirable. The fact that it is capable of accomplishing this end has been demonstrated in these studies. A potential field of usefulness, though as yet untested, might be found in the maintenance of an even level of anesthesia in patients to whom curare has been administered. There is now sufficient evidence that for practical purposes curare will have little or no influence on the functioning of the method under discussion. Second, if therapeutic value should be indicated in the prolonged maintenance of narcosis, it is reasonable to assume that this method might be adapted to that purpose. At present we are unaware of any recognized therapeutic procedures involving prolonged narcosis with the agents used to the present time. Third, perhaps the greatest immediate value to be derived from the use of this method lies in the field of its research application. There long has been a need for a definite objective control of anesthesia in many of the problems encountered in pharmacologic and physiologic investigations. Often the uncertainty introduced by the necessity of maintaining animals under anesthesia of uncalculated depths has an important bearing on the conclusions derived from the experiment. Up to the present time this variable has been controlled by the interpretation of certain isolated reflex phenomena which in themselves are notably inconstant. In addition to these research applications it is our belief that this method may constitute a valuable tool in the elucidation of the fundamental nature of anesthesia in the higher species of animal life. Fourth, in a more general way it is considered that the development of automatic control of anesthesia, which is an example of the application of the servomechanism theory, opens wide and interesting possibilities of automatic control in the entire field of medicine.

DR. WILLIAM L. ESTES JR., Bethlehem, Pa.: My only qualification to discuss this report is that I have seen this remarkable machine in action. It is most uncanny and dramatic to observe the automatic record of the patient's condition unfold, including both the electrocardiographic changes and the electroencephalographic record, while the little click every few seconds indicates likewise the automatic administration of small increments of the anesthetic agent. The mechanism by which all this is accomplished is most baffling to a mere surgeon. Although the full significance of a machine of this character in the field of anesthesia is at this time difficult to predict, the immediate potentialities are most impressive and seem epoch making. It is of extreme value and importance that study of the encephalographic patterns elaborated by this apparatus indicates that the changes in pattern follow the degree or depth of anesthesia and that from the stage of loss of consciousness with any increase in depth of anesthesia, the energy output of brain waves is gradually decreased. With the great advances in anesthesia in the last decade one has been impressed by the fact that the problems of anoxemia and of cardiac and respiratory arrest in the patient under anesthesia in no way seem to have been abolished. Some of the underlying etiological factors for lethal complications may lie either (1) in the increasing tendency to use and the apparent vogue for use of multiple anesthetic or analgesic agents in a single patient, or (2) in the idiosyncrasy of the patient to one or more of the drugs employed and abnormal reaction to minimal or conventional dosage. Present methods of measuring the effect of the anesthetic on the patient and of estimating the depth of anesthesia are relatively crude—simple recording of the pulse, respiratory rate and blood pressure or observing reflexes—and, as Dr. Mayo has pointed out, estimation of depth of anesthesia by these means is an art rather than a science. One step toward more accurate estimation of anesthetic effect has been the oximeter of McClure and his co-workers. And now this machine presented by Drs. Mayo, Bickford and Faulconer, while seemingly highly technical, provides an accurate and scientific record of the vital functions of a patient under anesthesia and a prompt indication of early deviation from the normal and thus will indicate the need for therapy to prevent impending serious complications or disaster far quicker and earlier than any previous means or modality. It would also seem that this method of recording a patient's physical functions opens up a new field of more scientific approach to gaging the effect of anesthetics and surgical procedures on patients and offers untold potentialities toward advancing our knowledge of the detailed effects of anesthetics as well as rendering their administration far more safe.

DR. R. G. BICKFORD, Rochester, Minn.: This method of anesthesia control consists essentially of the application to the human of engineering principles that have been known since James Watt invented the governor for his steam engine. This type of control system, known technically as a servomechanism and exemplified by a household thermostat, was studied a great deal in the last war and the information gained was used in the construction of robot missiles and other automatic weapons. Many of the servomechanisms which exist in the human body have been described by Claude Bernard and later by Walter Cannon under the general term "internal hemostasis." What we have attempted in automatic anesthesia is to apply an external regulating system to the human body. This may be looked on as a form of "external hemostasis." The simple injection technic described has application outside the field of anesthesia for the control of the concentration of chemical substances in the blood. For instance, anticonvulsive drugs can be automatically administered until seizure activity disappears from the brain. If the sensing element is replaced by a Geiger counter, the system could be used to maintain a desired concentration of a radioactive substance, for example, radioactive iodine in the thyroid. We are hoping to explore some of these applications in the near future.

INTRAVENOUSLY ADMINISTERED SACCHARATED IRON OXIDE IN THE TREATMENT OF HYPOCHROMIC ANEMIA

Therapeutic Results, Potential Dangers and Indications

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Saccharated iron oxide given intravenously has recently been used successfully by several groups of British investigators for the treatment of iron deficiency anemia.[1] The therapeutic response has been uniformly good; reactions have been both infrequent and mild. It is surprising that the preparation can be injected with relative safety since all other forms of iron administered parenterally have caused reactions so severe that their use had to be abandoned; these include ferrous citrate, iron citrate green, ferrous gluconate, ferrous ascorbate, colloidal ferric hydroxide and colloidal ferric oxide.[2] The toxic manifestations commonly observed with the last two compounds were nausea, vomiting, abdominal and lower back pain, lacrimation, nasal stuffiness, headache, flushing and swelling of the face, swelling and stiffness of the tongue, paresthesias, fever, rapid fall in systolic blood pressure, substernal pain and a sense of impending death. The earlier studies with these therapeutically unsatisfactory iron preparations, however, had demonstrated that injected iron is almost quantitatively converted into hemoglobin; and when the amount of injected iron is large (0.608 to 1.32 Gm.) the reticulocyte response is dramatic and the rate of hemoglobin regeneration maximal.[2b] For these reasons the discovery of a safe, effective form of parenteral iron therapy must be regarded as important. At the same time, it should be emphasized that there are few legitimate indications for the injection of iron since almost all iron-deficient patients respond well to oral therapy. Furthermore, if the dose is not carefully calculated, much larger amounts of saccharated iron oxide may be given than are needed to correct the deficiency, and excessive, potentially harmful deposits of iron in tissues may result.

The present report (1) describes the clinical and hematological responses of 10 patients with hypochromic microcytic anemia to the intravenous administration of saccharated iron oxide, (2) emphasizes the potential toxic effects of overdosage and (3) defines the indications for the use of saccharated iron oxide.

THERAPEUTIC RESPONSE TO INTRAVENOUSLY ADMINISTERED SACCHARATED IRON OXIDE

Saccharated iron oxide was given intravenously to 10 patients with hypochromic microcytic anemia. (See the accompanying table). The primary cause of iron deficiency in each instance was hemorrhage either from the uterus or from the gastrointestinal tract. Hypochlorhydria and poor diet were undoubtedly important contributory causes in several patients. Initial hematological values showed the following range of variations: red blood cells, 3.14 to 5.17 million cells per cubic millimeter; hemoglobin 5.8 to 9.8 Gm. per 100 cc., and mean corpuscular hemoglobin concentration, 25 to 31 per cent.

Three different preparations of saccharated iron oxide, each made by a different manufacturer, were used.[3] They contained 100 mg. of iron per 5 cc. According to Mannich and Rojahn,[4] saccharated iron oxide is a negatively charged colloidal solution of ferric hydroxide, stabilized by adsorption of alkali and sugar. The methods by which these commercial preparations are made and their exact chemical compositions have not been announced. The three solutions were equally effective, however, and equally free of side reactions. Some patients received 40 mg. of iron the first day, 60 mg. the second day and 100 mg. daily thereafter; in a few instances the initial dose was 100 mg. A few patients were given 200 mg. at a time, and occasionally the dose was repeated twice during a 24 hour period. The total dosage varied from 700 to 2,000 mg. Injections were made through a 20 gage needle into an antecubital vein, care being taken to avoid any leakage outside the vein. After it became evident that the material did not cause thromboses, the time of administration was often shortened to 15 to 30 seconds.

Each patient showed an excellent clinical and hematological response. Within several days after the start of therapy, patients noted improved appetites. Shortly thereafter, weakness became less pronounced. A reticulocyte peak occurred in all cases within six to 11 days; it was greater than 15 per cent in all but three patients and in one case reached a level of 21.2 per cent. The average daily rise of hemoglobin varied from 0.106 to 0.262 Gm. per 100 cc.; the over-all average rise for 10 patients was 0.177 Gm. per 100 cc. These data are summarized in the table. The response in one patient is shown graphically in figure 1.

Reactions were minimal. One patient (K. M.) complained of nausea, abdominal cramps and a chill after receiving her first dose of 100 mg. of iron as saccharated iron oxide. Subsequently, the dose was reduced to 40 mg. and gradually increased to the original 100 mg. without further reaction. Another woman (T. P.) reported transient pain along the course of the injected vein, due presumably to venous spasm. In a third subject with exceedingly small veins (E. C.) several

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1. (a) Nissim, J. A.: Intravenous Administration of Iron, Lancet **2**: 49, 1947. (b) Davidson, L. S. P., and Girdwood, R. H.: Refractory Iron Deficiency Anaemia Treated with Intravenous Saccharated Oxide of Iron, Brit. M. J. **1**: 733, 1948. (c) Slack, H. G. B., and Wilkinson, J. F.: Intravenous Treatment of Anaemia with an Iron-Sucrose Preparation, Lancet **1**: 11, 1949. (d) Govan, A. D. T., and Scott, J. M.: Intravenous Iron in the Treatment of Anaemia of Pregnancy, ibid. **1**: 14, 1949. (e) French, D. G.: Intravenous Treatment of Anaemia with an Iron-Sucrose Preparation, ibid. **1**: 370, 1949. (f) Nissim, J. A., and Robson, J. M.: Intravenous Treatment of Anaemia with an Iron-Sucrose Preparation, ibid. **1**: 326, 1949; (g) Preparation and Standardization of Saccharated Iron Oxide for Intravenous Administration, ibid. **1**: 686, 1949. (h) Sinclair, R. J. G., and Duthie, J. J. R.: Intravenous Iron in Hypochromic Anaemia Associated with Rheumatoid Arthritis, ibid. **2**: 646, 1949.

2. (a) Stockman, R.: The Treatment of Chlorosis by Iron and Some Other Drugs, Brit. M. J. **1**: 881, 1893. Heath, C. W.; Strauss, M. B., and Castle, W. B.: Quantitative Aspects of Iron Deficiency in Hypochromic Anemia: (The Parenteral Administration of Iron), J. Clin. Investigation **11**: 1293, 1932. Reznikoff, P., and Goebel, W. F.: The Use of Ferrous Gluconate in the Treatment of Hypochromic Anemia, ibid. **16**: 547, 1937. Friend, D. G.: Iron Ascorbate in the Treatment of Anemia, New England J. Med. **219**: 910, 1938. (b) Goetsch, A. T.; Moore, C. V., and Minnich, V.: Observations on the Effect of Massive Doses of Iron Given Intravenously to Patients with Hypochromic Anemia, Blood **1**: 129, 1946.

3. The medical research divisions of three pharmaceutical companies supplied the iron solutions: (a) feojectin® by Smith, Kline & French Laboratories; (b) "intravenous iron, iron solubilized with sucrose" by the Wm. S. Merrell Company, and (c) "saccharated iron oxide" by Sharp & Dohme, Inc.

4. Mannich, C., and Rojahn, C. A.: Über die kolloide Natur des Eisenzuckers, Ber. d. deutsch. pharm. Gesellsch. **32**: 158, 1922.

milliliters of the solution were accidentally injected outside the vein; the area became indurated, hot, swollen and painful. Acute discomfort subsided after 96 hours, but the induration took several weeks to disappear. There were no thromboses in spite of the fact that several patients received all injections into the same vein. Patients frequently reported that they felt abnormally sleepy for 10 to 15 minutes after receiving an injection.

a variable degree in other subjects, and it has been noted after use of each of the three iron preparations. The transient leukopenia is of no clinical import; its mechanism is unknown.

POTENTIAL TOXIC EFFECTS OF OVERDOSAGE

The clinical experience reported by several groups of investigators [5] and that described in the preceding section establish the fact that up to 200 mg. of iron as

Response of Patients with Hypochromic Anemia to Intravenously Administered Saccharated Iron Oxide

Case No.	Patient	Age	Sex	Cause of Anemia	Initial Red Cell Constants *	Day of Therapy	RBC (10^6)	Hb. (Gm.)	Retics., %	Total Mg. of Iron Injected	Daily Rise in Hb. Gm. per 100 Cc.
1	K. M.	43	F	Gastrointestinal bleeding	MCV 66 MCHb. 22 MCHb.C 31%	−2 0 7 11 20 31	3.99 4.04 4.37 4.59 4.88 4.84	8.0 8.2† 8.8 9.7 11.5† 12.1	4.9 4.0 11.2 15.3 ... 3.4	1,340	0.167
2	H. G.	47	M	Bleeding hemorrhoids	MCV 67 MCHb. 18 MCHb.C 27%	−5 0 6 10 19	4.00 4.42 4.51 5.09 5.29	7.8 7.7† 9.6 10.1 11.7†	4.0 5.6 19.7 12.5 2.0	1,100	0.210
3	A. J.	16	F	Nutritional? menorrhagia	MCV 60 MCHb. 17 MCHb.C 29%	−3 0 5 9 27 41	4.00 3.73 4.22 4.04 3.99 4.83	7.1 7.1† 7.8 8.6 12.5† 12.7	2.9 3.3 11.9 15.8 4.7 1.6	1,100	0.200
4	D. H.	66	F	Bleeding diaphragmatic hernia	MCV 72 MCHb. 22 MCHb.C 31%	−2 0 5 10 49	3.73 4.02 3.81 4.28 4.37	8.3† 8.7 8.6 10.0† 11.3	7.7 5.6 12.3 20.2 ...	1,486	0.170
5	T. P.	46	F	Nutritional? menorrhagia	MCV 65 MCHb. 19 MCHb.C 30%	−2 0 7 14 34	3.98 4.41 4.55 4.61 4.72	8.5 8.9† 10.3 11.1† 12.3	4.6 5.8 19.8 10.5 2.4	900	0.157
6	E. B.	26	F	Menorrhagia; postpartum hemorrhage	MCV 71 MCHb. 22 MCHb.C 31%	−4 0 5 11 96	4.62 4.49 4.69 4.47 4.34	9.9 9.8 10.2 9.8 12.8	2.1 2.1 5.4 8.4 1.2	700	.....
7	E. S.	29	F	Menorrhagia, nutritional?	MCV 59 MCHb. 16 MCHb.C 27%	−3 0 8 23 24	4.95 5.17 5.10 4.44 5.34	7.4 7.5† 9.2 11.3† 13.0	... ... 15.7 2.8 2.2	1,700	0.165
8	E. C.	35	F	Menorrhagia	MCV 66 MCHb. 17 MCHb.C 25%	−3 0 5 9 29 77	3.24 3.14 3.67 3.54 4.04 4.37	6.0 6.0† 7.3 7.4 10.4† 13.1	3.4 3.4 11.8 16.3 1.0 6.0	1,000	0.158
9	V. L.	64	M	Bleeding hemorrhoids	MCV 67 MCHb. 16 MCHb.C 25%	−2 0 5 8 16 29	3.45 3.35 3.77 3.70 4.47 4.52	5.7 5.8† 6.9 9.0 10.9 13.4†	3.1 1.4 12.2 21.2 11.0 2.0	2,000	0.282
10	B. G.	29	F	Menorrhagia	MCV 70 MCHb. 21 MCHb.C 30%	−4 0 4 8 17 31 53	3.83 3.80 3.98 3.80 4.43 4.76 4.22	8.3 8.0 8.6 8.4 10.1 11.3 11.8	2.3 2.4 8.6 10.9 8.4 4.2 1.0	1,700	0.106

* The letters MCV, MCHb. and MCHb.C denote mean corpuscular volume, mean corpuscular hemoglobin and mean corpuscular hemoglobin concentration, respectively.
† Values from which average daily hemoglobin rise was calculated.

An interesting effect of these preparations was discovered accidentally. Blood counts were usually obtained daily on each patient immediately before the iron was given. One day, on E. S., blood was drawn into diluting pipets immediately after the iron injection; the counts showed a profound granulocytic leukopenia (1,000 white blood cells per cubic millimeter with only 10 per cent granulocytes). More detailed study then revealed that the leukopenia was extremely transient. It appeared within five minutes after the iron administration but persisted for less than 30 minutes. The same phenomenon has been observed repeatedly but to

saccharated iron oxide may be injected intravenously at one time with a high degree of safety for the patient. In all these studies great care was taken to give only enough iron to correct the deficiency. However, iron is often prescribed for patients who do not have hypochromic (iron deficiency) anemia, and its administration is frequently continued for months or years. If the same practice were followed for saccharated iron oxide,

5. (a) Holly, R. G.: Intravenous Iron Therapy, Bull. Univ. Minnesota Hosp. & Minnesota M. Found. **21**: 83, 1949. (b) Horrigan, D. L.; Mueller, J. F., and Vilter, R. W.: Observations on the Intravenous Administration of Saccharated Oxide of Iron in Human Beings, J. Lab. & Clin. Med. **36**: 422, 1950. (c) Footnote 1.

one could easily inject much greater amounts of the metal than are normally contained in the body. For instance, one injection of 5 cc. of saccharated iron oxide (100 mg. iron) each week for a year would provide over 5 Gm. of iron, an amount roughly equivalent to all the iron in the blood and tissues of an average normal adult man. More serious abuse with two or three such injections per week would provide 10 or 15 Gm. It is known that only small amounts of iron are excreted by the body except through hemorrhage. Consequently, the injected iron would be retained in large part and might eventually produce toxic effects. Since, to date, excessive amounts of iron have never been given to human subjects, one must evaluate the seriousness of the danger (*a*) by reviewing those situations in which iron has accumulated under pathological circumstances in the tissues of patients and (*b*) by animal experimentation.

Large accumulations of iron have been observed in the tissues of human subjects in the following circumstances: (*a*) in hemochromatosis; (*b*) after a large number of transfusions, and (*c*) in adult Bantu natives of South Africa who live almost exclusively on maize diets and have chronic nutritional deficiencies. For the sake of comparison later, the following features of

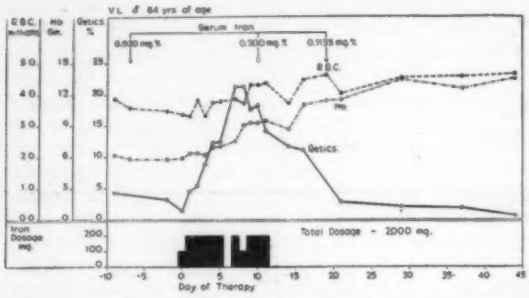

Fig. 1.—Response of V. L., a man aged 64, to 2,000 mg. of iron as saccharated iron oxide, given intravenously in 100 and 200 mg. daily doses to this patient with iron deficiency anemia. A reticulocyte peak of 21.2 per cent was attained after seven days of iron administration, and a corresponding rise in hemoglobin and erythrocyte values was subsequently seen. Serum iron rose from low values before treatment to normal values within three weeks.

hemochromatosis are emphasized here: it occurs predominantly in adult males; is of unknown causation but probably related to an inborn error of iron metabolism; is characterized by excessive deposits of hemosiderin and hemofuscin in the liver, pancreas and other tissues, and is frequently associated with hepatomegaly, cirrhosis, diabetes and bronzing of the skin.

Thirty cases of transfusion hemosiderosis have been described in the literature[6]; we have observed 10 additional patients, four of whom are still living. These 40 cases are essentially of three types: (*a*) pernicious anemia seen before the advent of liver therapy; (*b*) hypoplastic anemia, and (*c*) chronic forms of leukemia. In the reported patients the number of transfusions has varied between 12 and 290; one of our living subjects has received 534. If it is assumed that each transfusion averaged 500 cc. and that the amount of iron per 100 cc. of transfused blood averaged 50 mg., then the total amount of iron given to these subjects as hemoglobin varied from about 3 to 130 Gm. Hepatic enlargement was a frequent but not invariable result of these multiple transfusions, but fibrosis and cirrhosis were comparatively slight. Bronzing of the skin was usually noted in the subjects who received the larger quantities of blood. Diabetes was present in only six instances; in one case it appeared to be incidental, while in two others the only evidence for diabetes was an elevated fasting blood sugar level. There were mild to moderate amounts of hemosiderin in the spleen, pancreas, periportal lymph nodes, kidneys, adrenals and cardiac muscle with little evidence of fibrous tissue reaction. In six of the nine adults observed by us there were manifestations of cardiac failure.

Some clinical investigators have emphasized the similarity between transfusion hemosiderosis and hemochromatosis.[6b] There are differences, however, which seem important. Even though iron in the hepatic cells is definitely increased in transfusion hemosiderosis, the greatest deposits in liver and other tissues are in cells of the reticuloendothelial system. In hemochromatosis, by contrast, the iron deposition is largely parenchymal. Other differences include the infrequency of diabetes and the inconstant presence of true portal cirrhosis in transfusion hemosiderosis. More important than the relationship of these two disease states to each other, however, is the question whether the iron deposits actually cause the disturbances in hepatic, pancreatic and cardiac functions which do occur in hemosiderosis, no matter how inconstant. Since the deposition of iron from red cells which have been transfused into normal experimental animals does not produce fibrosis of the liver,[7] there appear to be other factors which cause the hepatic damage observed: the anemia itself, unrecognized serum hepatitis transmitted by one of the many transfusions or, in the case of hypoplastic anemia, hepatotoxic effects produced by the agents responsible for the marrow damage. About the only statements that may be made concerning the occasional association of diabetes with transfusion hemosiderosis are that the development of diabetes cannot be correlated with the number of transfusions and that it may be incidental. Chronic myocardial failure has never been observed in experimental animals given numerous transfusions. The patients with hemosiderosis in whom cardiac damage develops have usually had moderate to severe degrees of anemia for years and are often in the age group in which coronary artery disease is frequent. In spite of these considerations, and even though iron deposition in the myocardium is not great, one must assume until evidence to the contrary is produced that the iron is partly responsible for the disturbed cardiac function.

The third example of excessive deposition of iron in human subjects was described by the Gillmans[8] as cytosiderosis.[9] Cytosiderosis occurs in young adults of either sex among pellagrous Bantu natives whose food consists almost entirely of maize. The large amounts

6. (*a*) Yates, J. L., and Thalhimer, W.: Treatment of Pernicious Anemia: A Patient Who Received 113 Transfusions, J. A. M. A. **87**: 2156 (Dec. 26) 1926. (*b*) Schwartz, S. O., and Blumenthal, S. A.: Exogenous Hemochromatosis Resulting from Blood Transfusions, Blood **3**: 617, 1948. (*c*) Muirhead, E. E.; Crass, G.; Jones, F., and Hill, J. M.: Iron Overload (Hemosiderosis) Aggravated by Blood Transfusions, Arch. Int. Med. **83**: 477 (May) 1949. Hahn, A., and Bauer, J.: Personal communication to the authors. Wyatt, J. P., and Goldenberg, H.: Hemosiderosis in Refractory Anemia, Arch. Int. Med. **83**: 67 (Jan.) 1949. Wyatt, J. P., and Moraques, V. M.: Transfusional Siderosis, Am. J. Path., to be published.

7. Rous, P., and Oliver, J.: Experimental Hemochromatosis, J. Exper. Med. **28**: 629, 1918.

8. Gillman, J., and Gillman, T.: Structure of Liver in Pellagra, Arch. Path. **40**: 239 (Oct.) 1945. Gillman, J.; Mandelstam, J., and Gillman, T.: A Comparison of Chemical and Histological Estimations of the Iron and Copper Content of the Livers of Africans in Relation to the Pathogenesis of Cytosiderosis and Cirrhosis (Haemochromatosis), South African J. M. Sc. **10**: 109, 1945. Gillman, J., and Gillman, T.: The Pathogenesis of Cytosiderosis (Hemochromatosis) as Evidenced in Malnourished Africans, Gastroenterology **8**: 19, 1947.

9. The term cytosiderosis is used in this paper to refer specifically to the syndrome which the Gillmans[8] described and not as a synonym for hemochromatosis.

of inorganic iron in the diet apparently come from cooking utensils, and at least one of the factors which promotes excessive iron absorption is the low phosphorus content of the maize.[10] This disease is associated with hepatomegaly and varying degrees of portal cirrhosis; hemosiderin and hemofuscin may be found in large aggregates in the portal tracts. Intensely pigmented livers did not regularly show fibrosis, but in other instances cirrhosis was found superimposed on mild degrees of pigmentation.[8] There was no close correlation between the cirrhotic changes and the amount of iron present. For this reason, it is difficult to incriminate the iron as the cause of the fibrotic change. The Gillmans stated that many patients showed "a profound disturbance of carbohydrate metabolism" but cited no specific instance of diabetes and presented no histological studies of pancreatic tissue.

From the above discussion it is clear that in hemochromatosis, transfusion hemosiderosis and cytosiderosis excessive amounts of iron are associated with pathological changes in several organs, but it is not certain in any instance that the iron is actually responsible for precipitating these abnormalities. It is necessary, therefore, to seek further information from the controlled experiments possible with animal studies. In extensive long-term investigations Polson [11] injected a colloidal iron preparation into rabbits and Cappell [12] injected saccharated iron oxide into mice and rats. In the latter experiments as much as 550 mg. of iron per kilogram of body weight was given. Both authors studied the tissue distribution of iron in detail. In addition they observed that: (*a*) there was no tendency for the development of hepatic fibrosis; (*b*) no iron was deposited in the pancreas except in histiocytes, and (*c*) pancreatic fibrosis did not occur.

It seemed desirable to repeat these observations using the same saccharated iron oxide solutions now being used for the treatment of human subjects. Accordingly, saccharated iron oxide at two dosage levels (0.5 and 1.0 Gm. of iron per kilogram of body weight) was given intravenously to four dogs. The amount injected daily varied from 100 to 300 mg. of iron; the time required for administration of the total quantity (4.54 to 9.44 Gm.) varied from 44 to 68 days. The levels of 0.5 and 1.0 Gm. per kilogram correspond roughly to 35 and 70 Gm. of iron for an adult human of average size and equal or exceed the amounts usually found in the tissues of patients with hemochromatosis. These animals have been fed a diet of purina® dog chow and have now been carefully followed for a period of 15 months. They are active and healthy in appearance. Weight has either remained constant or increased slightly. Hematological values have remained normal. The serum bilirubin levels and the sulfobromophthalein sodium clearance test of hepatic function have showed no change. Fasting blood sugar levels have consistently been within normal limits. Serum iron values were high during the period of injection but returned to the upper range of normal after all the iron had been given. Electrocardiographic tracings have been within normal limits. Data collected during the first eight months of observation on one of the dogs are summarized in figure 2.

Biopsy specimens, before and six months after the injections were begun, were obtained from the liver, spleen, pancreas, mesenteric lymph nodes, skeletal muscle and skin. The control sections showed no histological abnormalities. Those taken at six months revealed pronounced iron pigmentation of the liver, spleen and mesenteric lymph nodes, with less pigment in the pancreas, kidney and skin, but practically none in skeletal muscle. There was no increase in fibrous tissue in the liver, pancreas or other organs, and there were absolutely no cirrhotic changes. Sections of the liver stained for iron revealed the hemosiderin to be deposited in coarse granules aggregated into clumps with focal distribution in the sinusoids and portal triads. In addition to these larger deposits there was a diffuse, fine, granular deposition of iron in the hepatic parenchymal cells throughout the lobules and in individual Kupffer cells. Smaller deposits of iron were seen in the endothelium of the blood vessels, but none was found in the bile ducts. In the spleen, the iron was found in large quantities in the macrophages of the sinusoids and to a lesser extent in the capsule, trabeculae and beneath the endothelium of the blood vessels. There

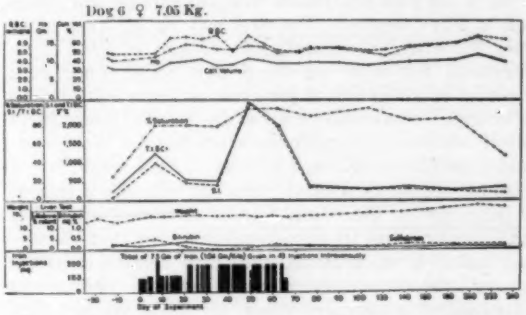

Fig. 2.—Response of dog weighing 7.05 Kg. to 7.3 Gm. (1.04 Gm. per kilogram of body weight) of iron as saccharated iron oxide given intravenously in divided doses during a period of 66 days. There were no significant changes in erythrocyte values, serum bilirubin or hepatic function as measured by sulfobromophthalein sodium clearance. The weight increased slightly during the 240 days of observation. The serum iron level rose to high values during the period of injections but fell to the higher limits of normal after the injections were completed though the percentage of saturation remained elevated. The letters S. I. and T. I. B. C. denote serum iron and total iron-binding capacity.

were small amounts of iron in the glomerular capillary tufts with faint diffuse deposits and rare fine granules in the renal tubules. The pancreas revealed only small amounts of iron confined to macrophages and to the subendothelial layers of the blood vessels. None was detectable in the acini or islet epithelial cells. Mesenteric lymph nodes showed large quantities of iron deposited in the macrophages in the central sinusoids with a less decided pigmentation of the peripherally located macrophages. Iron in the skin was confined to macrophages in the dermis, especially those around hair follicles; there was no pigmentation of the epidermis. The only iron seen in skeletal muscle sections was a trace in the endothelium of some capillaries. No pigment resembling hemofuscin was found in any of the sections.

In the animal experiments just described there was no clinical, laboratory or histological evidence of any dysfunction produced by the injected iron. The periods of observation, however, were relatively short. It remains entirely possible that large tissue deposits of iron may cause anatomic or functional damage to organs

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11. Polson, C. J.: The Fate of Colloidal Iron Administered Intravenously, J. Path. & Bact. **31**: 445, 1928; The Fate of Colloidal Iron Administered Intravenously: Long Experiments, ibid. **32**: 247, 1929; The Failure of Prolonged Administration of Iron to Cause Haemochromatosis, Brit. J. Exper. Path. **14**: 73, 1933.

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not after 1 or 2 years but after 5 or 10. Until this possibility can be eliminated by further study, it is highly important that the injection of excessive amounts of iron into human subjects be diligently avoided.

INDICATIONS FOR THE USE OF INTRAVENOUS IRON THERAPY

Since the response of patients with hypochromic anemia to oral iron therapy is so uniformly good, there are few real indications for giving iron parenterally. It is true that many persons have mild gastrointestinal discomfort when oral therapy is begun; but if the initial doses are small and increased gradually over a period of three or four days to the usual therapeutic amounts, almost all patients can tolerate the iron. However, attention should be called to special situations in which parenterally given iron preparations will be helpful.

1. Hypochromic anemia in patients with ulcerative colitis, with functioning colostomy, after extensive bowel resection, and with sensitivity to iron. In these circumstances oral iron therapy may not be tolerated because gastrointestinal symptoms are severely aggravated or because sensitivity manifestations are produced. Two of our patients treated with saccharated iron oxide fell in this category. The first was K. M. (see table, case 1), a white woman aged 43, who in 1942 at an operation for acute intestinal obstruction underwent removal of a segment of gangrenous ileum infarcted by adhesions. Since the operation she has had intermittent bloody diarrhea, the cause for which has not been determined despite many examinations. As a result, hypochromic anemia developed. She has been given ferrous sulfate, ferrous gluconate, ferrous carbonate and other oral preparations on numerous occasions, but therapy has had to be discontinued each time because of severe nausea, abdominal cramps and diarrhea. The patient experienced a reaction when she received her first intravenous injection of saccharated iron oxide but tolerated subsequent injections well and had an excellent remission. The second patient was D. H. (case 4 on the table), a white woman aged 66 in whom hypochromic anemia appeared secondary to blood loss associated with a diaphragmatic hernia.[13] Oral ingestion of iron repeatedly caused itching of her skin and angioneurotic edema-like swelling of her face and hands. This woman sought relief from her anemia in a number of large medical centers. Each time her story of sensitivity to iron was greeted with skepticism, but each time the same manifestations appeared when any iron salt was taken by mouth. These symptoms were so intolerable that she refused to continue therapy. We gave her a test dose of radioactive iron (1 mg. per kilogram of body weight) in order to measure iron absorption; 25 per cent of the dose was absorbed, but the angioneurotic edema which appeared was unmistakable. Skin tests, patch tests and passive transfer tests done by Dr. Samuel Bukantz in an attempt to demonstrate the sensitivity were inconclusive. The initial dose of saccharated iron oxide given intravenously contained only 6 mg. of iron; the amount injected was then increased gradually to provide 24, 56, 100 and finally 200 mg. per day. There were no reactions whatever. Both clinical and hematological improvement was dramatic.

13. Dr. Charles A. Doan referred this patient to us.

2. Hypochromic anemia in patients refractory to oral therapy. Several patients have been reported who failed to respond to oral intake of iron but who made excellent recoveries after receiving saccharated iron oxide intravenously.[14] Presumably, they were not able to absorb iron from the gastrointestinal tract. In no instance, however, has definite proof of poor absorption been obtained. Absorption studies were not actually made, and there was no evidence except the patient's word that the oral iron preparations had actually been taken. These cases must be extremely rare; the authors have never seen one. It is conceivable that iron absorption may be exceedingly poor in steatorrhea or sprue. Undoubtedly, however, oral iron therapy fails most frequently because its use is not restricted, as it should be, to the treatment of hypochromic anemias.

Other legitimate indications for parenteral iron administration may become evident later. In particular, it is probable that one could give saccharated iron oxide intravenously to hypochromic, pregnant women seen for the first time only a few days before the expected date of delivery and that enough of the iron would pass the placental barrier to protect the infant from developing iron deficiency during the first year of life. We have treated two such patients, but the babies of these mothers are still in the newborn period. There has not been sufficient time to determine whether they will or will not become hypochromic.

It is evident that in only two of the 10 patients listed in the accompanying table was there good reason to give saccharated iron oxide intravenously. The other eight patients would almost certainly have responded well to oral therapy. The parenteral iron was given only because its safety and effectiveness were being evaluated. As long as the total dose is carefully regulated, however, there are no known scientific reasons why it should not be used in any hypochromic patient. Practically, it would probably be more expensive to the patient and often considerably less convenient.

COMMENT

Saccharated iron oxide, given intravenously, has produced satisfactory hematologic and clinical remissions in patients with uncomplicated hypochromic anemia,[15] hypochromic anemia associated with pregnancy[16] and hypochromic anemia appearing in subjects with rheumatoid arthritis.[1h] Most authors have recommended that the initial dose be 20 to 50 mg. of iron and that the daily dose thereafter be 100 or 200 mg. until the deficiency is corrected. The total dose to be given can be calculated by using either of the following simple formulas:

$$\frac{\text{Norm. Hb.} - \text{Init. Hb.}}{100} \times \text{Blood Volume in cc.} \times 0.0034 \times 1.5 = \text{Fe}_4$$

where: (1) The normal hemoglobin is assumed to be 15 Gm. for men and 13.5 Gm. per 100 cc. for women.

(2) Blood volume is estimated to be 80 cc./Kg. body weight.

(3) The factor 0.0034 converts grams of hemoglobin into grams of iron.

(4) The factor 1.5 is arbitrarily employed to provide for extra iron to replace the depleted tissue stores.

(5) Fe_4 is the calculated dose in grams of iron.

14. Davidson and Girdwood.[1b] Slack and Wilkinson.[1c] Sinclair and Duthie.[1h] Horrigan, Mueller and Vilter.[1b]

15. Nissim.[1a] Davidson and Girdwood.[1b] Slack and Wilkinson.[1c] French.[1e] Nissim and Robson.[1f] Horrigan, Mueller and Vilter.[1b]

16. Govan and Scott.[1d] Holly.[1a]

If one assumes that the body volume is 5,000 cc., he may multiply $\frac{5.000}{100}$ by 0.0034 by 1.5 to obtain the factor 0.255. The formula for determining the total dose may then be simplified to become:

(Normal hemoglobin — Initial hemoglobin) × 0.255 = Fe_4

Hemoglobin values are used in terms of grams per 100 cc., not percentage of normal.

Within three or four days after injections of the saccharated iron oxide are begun, patients usually experience a sense of well-being, and reticulocytes in the peripheral blood begin to increase. The reticulocyte peak is reached in six to 11 days and is usually higher than with oral therapy. Hemoglobin values begin to rise about the end of the first week; the rate of hemoglobin regeneration is maximal.[2b] In the ten patients reported in this study, it varied from 0.106 to 0.262 Gm. per 100 cc. per day.

Reactions to saccharated iron oxide have been minimal. In a few of the reported cases generalized toxic reactions of mild degree have occurred[17]; several of these were observed, however, with solutions made by the investigators themselves rather than with the more carefully standardized commercial preparations. Thromboses and venous spasm have been observed in a few instances.[18] The incidence of reactions apparently rises as the individual dose is increased above 200 mg. In our 10 treated patients there was only one generalized reaction. One patient complained of transient pain along the course of the injected vein. Leakage of the saccharated iron oxide outside the vein caused a painful induration in one instance, but the lesion slowly disappeared without complication. We have noted two effects not previously described: (1) a transient, severe granulocytic leukopenia during the first 15 to 20 minutes after injection and for 10 to 15 minutes after it has been completed. No attempt is made to minimize the importance of these reactions. Their mildness is impressive only because other forms of parenteral iron are so much more toxic. None of the reported or observed reactions to saccharated iron oxide has been severe, but they are all troublesome.

Saccharated iron oxide, as a relatively safe parenteral iron preparation, is undoubtedly of value, but it does not represent a great therapeutic advance. Few patients are unable to tolerate or fail to respond satisfactorily to oral iron administration. Such patients in the past have been treated satisfactorily by transfusion of whole blood. There is, furthermore, the danger that saccharated iron oxide might be given in much larger amounts than are required to correct a deficiency or be given to persons who are not iron deficient. The excess iron will then be stored in tissues because the body is unable to excrete it; conceivably over a period of years it may produce fibrosis and functional changes in the liver, pancreas and other tissues. It must be admitted that the evidence attributing such chronic, toxic effects to large amounts of tissue iron is incomplete. In hemochromatosis, transfusion hemosiderosis and cytosiderosis the excessive iron deposits may be in no way responsible for the associated tissue changes, but one cannot yet be sure. The use of saccharated iron oxide, therefore, should be restricted to the treatment of iron-deficient patients. The dose to be injected must be calculated. The calculated dose should not be exceeded.

17. Nissim.[2a] Davidson and Girdwood.[1b] Slack and Wilkinson.[1c] Holly.[2a] Horrigan, Mueller and Vilter.[2b]
18. Slack and Wilkinson.[1c] Horrigan, Mueller and Vilter.[2b]

SUMMARY AND CONCLUSIONS

Excellent therapeutic results were obtained in 10 patients with chronic hypochromic anemia from calculated doses of saccharated iron oxide given intravenously. Blood values were restored completely to normal; rates of hemoglobin regeneration were maximal. Two of the patients had previously been unable to tolerate oral iron in therapeutic amounts. Reactions to saccharated iron oxide were infrequent and mild. These results confirm completely the reports of several British investigators on the efficacy of this form of iron therapy.

From animal experiments and from a review of the pertinent literature, it is concluded that no definite decision about the chronic, toxic effects of excessive deposits of iron in tissues can yet be reached. It is certainly possible that excessive deposits may produce tissue damage over a period of years. Because of this danger, it is imperative that saccharated iron oxide be given only to iron-deficient patients in a dose calculated to correct the deficiency.

There are relatively few specific indications for the parenteral administration of iron. However, when hypochromic anemia develops in patients with ulcerative colitis, with a functioning colostomy after extensive resection of the bowel or with sensitivity to iron (rare), oral therapy may so aggravate intestinal symptoms or may produce sensivity manifestations so troublesome that the parenteral use of saccharated iron oxide is preferable to oral therapy. In other patients who would respond satisfactorily to ordinary iron preparations given orally, saccharated iron oxide may be injected with relative safety if the dose is carefully calculated. From a practical point of view, its use in these patients does not seem desirable because: reactions, even though mild and infrequent, will prove troublesome; daily injections for 10 to 14 days will often be inconvenient, and the cost to the patient is likely to be considerably greater than that for oral therapy.

NOTE.—Since this paper was submitted for publication, the authors' attention has been called to the experience of Scandanavian workers with another form of iron which has been used parenterally. The preparation is marketed under the proprietary name ferrigen® by the Astra Co. of Sweden. The iron is said to be linked to a soluble, high-molecular carbohydrate, the compound being built in a manner similar to ferritin. Clinical experience with this material has been summarized by N. S. E. Andersson: (Experimental and Clinical Investigations into the effect of Parenterally Administered Iron, *Acta Med. Scandinav.*, supp., 241, 1950).

Groups and Clinics.—The ethical principles actuating and governing a group or clinic are exactly the same as those applicable to the individual. As a group or clinic is composed of individual physicians, each of whom, whether employer, employee or partner, is subject to the principles of ethics herein elaborated, the uniting into a business or professional organization does not relieve them either individually or as a group from the obligation they assume when entering the profession.

From the PRINCIPLES OF MEDICAL ETHICS of the American Medical Association.

Clinical Notes, Suggestions and New Instruments

FATAL VIRUS HEPATITIS OCCURRING IN AN INFANT THREE MONTHS OF AGE

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Philadelphia

Virus hepatitis, occurring as either infectious hepatitis or homologous serum hepatitis, is extremely rare in infants under 6 months of age. The following case report is of particular interest because of several possibilities in the causation and transmission of the disease.

The illness occurred 60 days after the administration of commercial irradiated blood plasma, and the mother of this infant had infectious hepatitis about three years prior to the birth of the baby.

REPORT OF CASE

History of Present Illness.—A boy 3 months of age was admitted to the Jewish Hospital, Philadelphia, June 20, 1950 with the complaint of jaundice of 24 hours' duration. Prior to this, from June 3 to 11, 1950, the baby had fever (ranging from 101 to 103 F.). The fever did not respond to adequate therapy with penicillin or sulfonamides. On June 9 the liver was noted to be 3.5 cm. below the right subcostal border. From June 11 to 19, 1950, the baby was asymptomatic; however, on the latter date the baby became jaundiced. He was promptly admitted to the hospital, where the jaundice rapidly became more intense. Coma and convulsions ensued, and death occurred 18 hours after admission. Laboratory data are given in the accompanying table.

Laboratory Data

	Date	White Blood Cells, %	Polymorphonuclear Cells, %	Lymphocytes, %	Monocytes, %
Hematologic data.....	3/22/50	14,800	82	18	..
	3/23/50	17,600	78	22	..
	3/24/50	23,400	87	13	..
	6/ 4/50	8,500	78	12	10
Blood culture.....	3/26/50	Negative after 10 days			
Serologic tests.....	3/22/50	Comb's test negative			
	3/26/50	Serologic test for syphilis negative			
Urinalysis.....	6/ 4/50	Trace of albumin			
	6/20/50	Urinary urobilinogen absent; urinary bile pigments 2+			
Blood chemical studies..	6/20/50	Thymol turbidity 7 units			
		Cephalin flocculation 4+			
		Serum bilirubin 15.1 mg./100 cc.			
		Total serum proteins 6.1 Gm./100 cc. (albumin 5.0 Gm., globulin 1.1 Gm.)			

Past History.—The baby was born March 22, 1950 of a full term normal delivery and weighed 6 pounds 8 ounces (2,948 Gm.). The only abnormality noted was a moderate right metatarsus varus. During the neonatal period the baby had troublesome forceful vomiting, which began as soon as oral feedings were attempted. Five per cent glucose water, a weak evaporated milk formula, skim milk and a soybean milk substitute formula were all vomited. A roentgenogram of the chest and abdomen as well as a gastrointestinal series using barium contrast mediums were all normal. An antispasmodic drug, atropine methyl nitrate, combined with the use of evaporated milk formula thickened with cereal offered partial relief. Because of the possibility that prepyloric edema was responsible for the continuation of symptoms, two intravenous infusions of commercial irradiated blood plasma, 50 cc. each, were administered on April 3 and 4, 1950. All equipment used in the infusion had been autoclaved according to standard hospital technic. There was prompt subsidence of all symptoms following the plasma infusions, and the baby was discharged from the hospital April 12, 1950 weighing 6 pounds 12 ounces (3,062 Gm.) on a maintenance dose of atropine methyl nitrate 0.1 mg. before each feeding and thick cereal feedings. The baby did well at home, weighing 10 pounds 12 ounces (4,876 Gm.) June 3, 1950, at which time the present illness began.

Family History.—There was a strong family history of allergy. The mother had hay fever, and the maternal aunt had severe multiple ingestant and inhalant allergies. The mother had had infectious hepatitis in 1947. She was Rh negative and the father Rh positive, but there was no evidence, laboratory or otherwise, of erythroblastosis. This was her first child.

Report of Necropsy.—At necropsy gross observation showed that the liver was enlarged, with the anterior margin 3 cm. below the xiphoid process of the sternum and 2.5 cm. below the costal margin in the right midclavicular line. The substance was mottled red and tan, congested and firm. In the gastrointestinal tract the stomach was distended with gas. The muscle layers, particularly of the cardiac end of the stomach, were hypertrophied. The duodenum was congested. The papilla of Vater was small but the lumen was patent. Peyer's patches were slightly swollen. The entire mucosa has a deeply roughened appearance. The ileum contained a small amount of blackish material resembling altered blood. The colon contained clay-colored feces. The gallbladder was rather small and contained a little bile and mucus, which was squeezed with difficulty through the papilla into the duodenum.

Microscopically the liver was almost unrecognizable. At least half of the liver cells had been destroyed. The remaining cells showed swollen vacuolated cytoplasm and degenerating nuclei. Fragments of liver cells were seen in the sinusoids. In the region of what had been portal spaces there were numbers of proliferating pseudo bile canaliculi, with occasional transition between these and liver cells. Sinuses were overdistended in many places. At some places there were small hemorrhages where the sinus walls had been destroyed. Inflammatory cells, mainly mononuclear, were scattered throughout the tissues, with an occasional polymorphonuclear leukocyte among them. Fibroblasts were fairly numerous, especially in the portal spaces where there was a beginning fibrosis.

COMMENT

It seems certain that the source of the infection was either irradiated blood plasma or a carrier state existent in the mother. Unfortunately no hospital records exists of the lot number of the plasma; however, it is likely that the finishing number was 5523 E. It is our understanding that several or more finishing numbers may be included in the same lot. Correspondence with the pharmaceutical concern revealed that the bulk of this material was furnished to hospitals in the vicinity of New York City during Autumn of 1949 and the winter of 1949-1950. No reports of homologous serum hepatitis have as yet been forthcoming concerning this supply of plasma.

Although the incubation period of 60 days seems to incriminate irradiated plasma as the source of infection, one cannot be positive without further proof. It is also possible that a carrier state existed in the mother; however, it is likely that in utero infection would have been disastrous to the fetus and that postnatal infection would have had a shorter incubation perior. To my knowledge the carrier state cannot be proved without the use of human volunteers.

It would seem wise to be circumspect regarding the use of plasma in infants and children and for general supportive therapy to utilize various protein hydrolysates instead of plasma. Whenever plasma, irradiated or otherwise, is administered the lot number should be scrupulously recorded for reference should the need arise.

SUMMARY

A case of fatal virus hepatitis occurring in an infant 3 months of age is reported. The etiologic basis is uncertain, but the evidence points to either irradiated blood plasma or a carrier state of the mother.

8261 Temple Road (19).

Autopsy and pathological reports were prepared by Dr. Helen Ingleby, Department of Pathology, Jewish Hospital.

CONTRIBUTION TO THE SURGICAL TREATMENT OF ASCITES

Modification of the Crosby-Cooney Technic

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and
I. ALFRED BRECKLER, M.D.
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The surgical treatment of ascites has been revived in recent years as a result of the technic popularized by Crosby and Cooney.[1] They employ a glass button to establish a communication between the intraperitoneal space and subcutaneous tissue. A small pyrex® spool with flanged ends is sutured to the rectus sheath so that it runs from the peritoneal cavity through rectus muscle to the subcutaneous fat. Ascitic fluid moves through the button and into a space between the rectus fascia and subcutaneous fat and is there absorbed. There is little doubt that for the purpose intended the technic is feasible and of great benefit to many patients burdened with severe ascites.

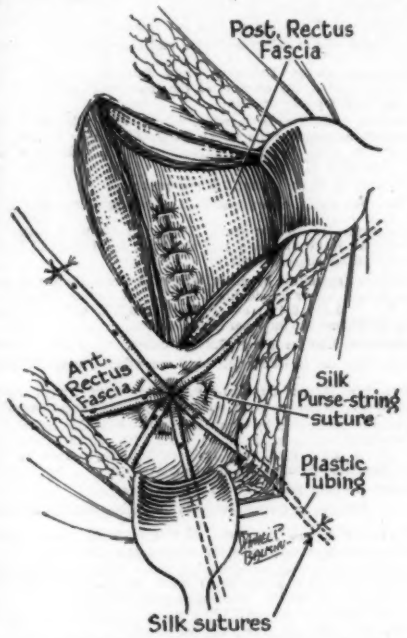

Fig. 1.—Posterior rectus fascia and peritoneum are closed. Note the purse-string suture around the bundle, placed in anterior rectus fascia, and the silk sutures tacking the tubing in place.

Schwei [2] has reported that 9 patients treated with the Crosby-Cooney button had remarkable control of their ascites. Warren [3] considered the method extremely beneficial. Unfortunately, as with every surgical procedure, there are instances of failure. Welch [4] studied 2 cases at autopsy and found that after two to four weeks the benefits obtained were negligible. He found that a subcutaneous cystic space with a dense fibrous wall had formed around the exit opening of the button and that effective absorption of fluid was almost completely impaired. Lord [5] has evidently heard of or seen similar failures, for he has tried stripping the rectus and external oblique fascia around the button to render the absorbing surface more reliable.

We have heard of similar difficulties with the glass button and have attempted to use another mechanical device to overcome the problem described. We employ a bundle of six polyethylene tubes (0.055 inches [1.4 mm.] inside diameter and 0.075 inches [2 mm.] outside diameter) approximately 6 inches (15 cm.) long. The tubing is bound together by two ties of surgical silk 1 inch (2.5 cm.) and 2 inches (5 cm.) from one end of the bundle.

Small holes are cut at intervals in the tubing. The bundle is then sterilized by boiling and inserted into the peritoneal cavity through rectus muscle and sheath as described by Crosby and Cooney.[1] The peritoneal end of the bundle has the shorter free ends, and the longer free tubes are then fanned out into the subcutaneous space, using as a guide a grooved director. (See figures 1 and 2 for exact technic.) We employ a plastic material which has been tissue tested in rabbits in our laboratories. It is nonirritating to tissue.[6]

It seemed to us that using tubing in this fashion would offer a much larger surface for absorption and that, being nonreactive, it would keep pocketing at a minimum. Our experience with this technic has been limited to 2 cases, but the results are sufficiently encouraging to warrant further trial.

REPORT OF CASES

CASE 1.—A white woman aged 57 had hepatic cirrhosis with increasing ascites, despite careful medical therapy, for a period of three years. Abdominal paracentesis was necessary with increasing frequency, until tapping was needed bimonthly prior

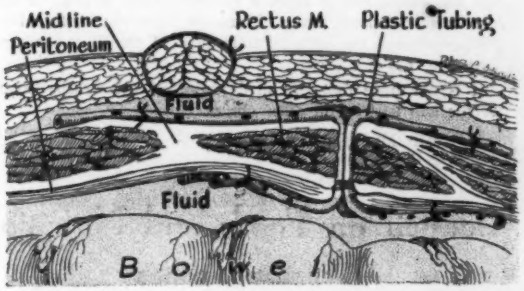

Fig. 2.—Cross section of the anterior abdominal wall showing the final position of the tubing within the abdominal cavity and under the subcutaneous layer.

to admission of the patient to the hospital. She suffered advanced malnutrition secondary to the severe cirrhosis and extreme generalized arteriosclerosis. There was severe ascites; the liver was palpable 5 fingerbreadths below the costal arch, and the spleen was definitely enlarged. Liver function studies showed pronounced hepatic damage.

After the insertion of the plastic tubing the patient remained hospitalized two weeks; successful convalescence was prevented by her general debilitation. Immediately after completion of the surgical procedure dependent edema developed over the sacral and pubic areas, and the anterior abdominal wall became decidedly edematous and remained so. Tapping was not necessary, although the abdomen seemed to increase slightly in size. The advanced state of senility and emaciation contributed to making the patient completely uncooperative, and she finally refused any type of nourishment. As a result, she died in coma seven weeks after the surgical intervention. Even in such an advanced stage of debility paracentesis was not required, and fluid continued to be absorbed to the time of her death.

CASE 2.—A white man aged 51 had enjoyed good health until the three weeks prior to admission. He had been on vacation and had been pleased with an 18 pound (8.2 Kg.) gain in weight. Abdominal swelling, tenderness and nausea brought

From the University of Illinois Medical School (Dr. Parker, Clinical Assistant Professor of Surgery) and from Michael Reese Hospital (Dr. Parker, Attending Surgeon, and Dr. Breckler, Surgical Resident).

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him to his physician. He had been a moderate but continuous drinker of whisky for many years. Physical examination revealed a tense abdomen, obviously containing fluid, and an enlarged liver. Studies of hepatic function showed severe impairment of hepatic metabolism.

A set of plastic tubes was inserted, and at the same time liver biopsy confirmed the diagnosis of cirrhosis. There was definite improvement for the two weeks following surgical intervention while the patient was in the hospital. Five weeks after the operation so much subcutaneous fluid had collected that it was necessary to withdraw 2 gallons (7.56 liters) of ascitic fluid from the superficial pocket formed after the surgical treatment. There was no evidence at that time of intra-abdominal fluid. For the next three weeks the fluid did not reaccumulate. The patient expired in coma from hepatic failure, about two months after the tubes were inserted.

In neither case did fibrosis produce pocketing of fluid within the first four to six weeks, as Welch [4] had mentioned observing with use of the glass button. Both patients had adequate amounts of fluid freely absorbed from the subcutaneous spaces.

SUMMARY AND CONCLUSION

Two patients with severe ascites, both of whom died after hepatic failure, were treated with the insertion of plastic tubing that extended from the abdominal cavity to the subcutaneous tissue of the anterior abdominal wall. In both instances ascitic fluid was present in copious amounts in the subcutaneous tissues for a period of seven weeks.

Both patients were near death when treated, and in neither instance was an autopsy obtained. However, it seemed to us that the plastic tubing allowed extremely free passage of fluid into the subcutaneous tissue. Moreover, even when both patients were moribund, the outward movement of the fluid continued. Pocketing did not occur.

It is our hope that this modification of the Crosby-Cooney technic will be tried in other clinics.

30 North Michigan Avenue.

Council on Foods and Nutrition

ACCEPTED FOODS

The following products have been accepted as conforming to the rules of the Council.

JAMES R. WILSON, M.D., *Secretary.*

Borcherdt Malt Extract Company, Chicago.

BORCHERDT MALT SOUP EXTRACT POWDER, COCOA FLAVORED, consists of malted barley extract, potassium carbonate and cocoa.

Analysis (submitted by manufacturer).—Moisture 3.60%, total solids 96.40%, ash 3.20%, protein 9.30%, fat 0.9%, maltose 67.50%, dextrins 12.80%, starch 0.62%, crude fiber 0.22% theobromine 0.09% and caffeine 0.03%.

Calories.—3.7 per gram; 105 per ounce.

Use.—For use as a mildly laxative food adjuvant in the diets of children.

Libby, McNeill & Libby, Chicago.

LIBBY'S STRAINED AND HOMOGENIZED CHICKEN SOUP consists of chicken broth, chicken, carrots, wheat starch, celery, onions, salt, parsley and monosodium glutamate.

Analysis (submitted by manufacturer).—Total solids 9.50%, moisture 90.5%, ash 0.36%, fat 1.34%, protein (N × 6.25) 0.83%, crude fiber 0.15%, carbohydrates other than crude fiber (by difference) 6.92%.

Vitamins and Minerals	Per 100 Gm.
Total vitamin A activity	760 I.U.
Thiamine	0.0049 mg.
Riboflavin	0.026 mg.
Nicotinic acid	0.35 mg.
Calcium	12.0 mg.
Phosphorus	12.0 mg.
Iron	2.5 mg.

Calories.—0.43 per gram; 12.2 per ounce.

Use.—For use in the feeding of infants, convalescents, and others requiring a soft diet.

Reid Murdoch & Company, Division of Consolidated Grocers Corporation, Chicago.

MONARCH BRAND DIETETIC PACK APRICOTS—UNPEELED HALVES consists of the fruit itself packed in water without any added sugar or salt.

Analysis (submitted by manufacturer).—Available carbohydrates (total carbohydrate minus crude fiber) 9.0%, fat (ether extract) 0.2%, protein (N × 6.25) 0.3%, ash (minerals) 0.5%, sodium 21 mg. per 100 Gm., potassium 156 mg. per 100 Gm.

Calories.—0.40 per gram; 11.3 per ounce.

Use.—For use in calory-restricted and other therapeutic diets.

MONARCH BRAND DIETETIC PACK ROYAL ANNE CHERRIES consists of the fruit itself, packed in water without any added sugar or salt.

Analysis (submitted by manufacturer).—Available carbohydrates (total carbohydrate minus crude fiber) 10.0%, fat (ether extract) 0.5%, protein (N × 6.25) 0.7%, ash (minerals) 0.3%, sodium 16 mg. per 100 Gm., potassium 101 mg. per 100 Gm.

Calories.—0.48 per gram; 13.6 per ounce.

Use.—For use in calory-restricted and other therapeutic diets.

MONARCH BRAND DIETETIC PACK FRUIT COCKTAIL consists of peaches, pears, grapes, pineapple and Maraschino type cherries, packed in water without any added sugar or salt.

Analysis (submitted by distributor).—Available carbohydrates (total carbohydrate minus crude fiber) 10.0%, fat (ether extract) 0.2%, protein (N × 6.25) 0.4%, ash (minerals) 0.2%, sodium 18 mg. per 100 Gm., potassium 90 mg. per 100 Gm.

Calories.—0.45 per gram; 12.8 per ounce.

Use.—For use in calory-restricted and other therapeutic diets.

MONARCH BRAND DIETETIC PACK PEACHES—YELLOW CLINGSTONE (SLICED OR HALVES) consists of the fruit itself, packed in water without any added sugar or salt.

Analysis (submitted by manufacturer).—Available carbohydrates (total carbohydrate minus crude fiber) 6.0%, fat (ether extract) 0.2%, protein (N × 6.25) 0.4%, ash (minerals) 0.2%, sodium 23 mg. per 100 Gm., potassium 97 mg. per 100 Gm.

Calories.—0.28 per gram; 7.9 per ounce.

Use.—For use in calory-restricted and other therapeutic diets.

MONARCH BRAND DIETETIC PACK PEACHES—ELBERTA FREESTONE (SLICED OR HALVES) consists of the fruit itself, packed in water without any added sugar or salt.

Analysis (submitted by manufacturer).—Available carbohydrates (total carbohydrate minus crude fiber) 6.0%, fat (ether extract) 0.2%, protein (N × 6.25) 0.4%, ash (minerals) 0.2%, sodium 21 mg. per 100 Gm., potassium 136 mg. per 100 Gm.

Calories.—0.28 per gram; 7.9 per ounce.

Use.—For use in calory-restricted and other therapeutic diets.

MONARCH BRAND DIETETIC PACK BARTLETT PEARS consists of the fruit itself, packed in water without any added sugar or salt.

Analysis (submitted by manufacturer).—Available carbohydrates (total carbohydrate minus crude fiber) 9.0%, fat (ether extract) 0.3%, protein (N × 6.25) 0.2%, ash (minerals) 0.2%, sodium 16 mg. per 100 Gm., potassium 51 mg. per 100 Gm.

Calories.—0.40 per gram; 11.3 per ounce.

Use.—For use in calory-restricted and other therapeutic diets.

MONARCH BRAND DIETETIC PACK CUT WAX BEANS consists of the vegetable itself, packed in water without any added salt.

Analysis (submitted by manufacturer).—Available carbohydrates (total carbohydrate minus crude fiber) 4.0%, fat (ether extract) 0.2%, protein (N × 6.25) 1.4%, ash (minerals) 0.7%, sodium 34 mg. per 100 Gm., potassium 97 mg. per 100 Gm.

Calories.—0.24 per gram; 6.8 per ounce.

Use.—For use in low sodium and other therapeutic diets.

MONARCH BRAND DIETETIC PACK SLICED CARROTS consists of Chantenay carrots, packed in water without any added salt.

Analysis (submitted by manufacturer).—Available carbohydrates (total carbohydrate minus crude fiber) 6.0%, fat (ether extract) 0.3%, protein (N × 6.25) 1.0%, ash (minerals) 0.6%, sodium 53 mg. per 100 Gm., potassium 78 mg. per 100 Gm.

Calories.—0.32 per gram; 9.1 per ounce.

Use.—For use in low sodium and other therapeutic diets.

Richmond-Chase Company, San Jose, Calif.

DIET-DELIGHT BRAND ASPARAGUS consists of the vegetable itself, packed in water without any added salt.

Analysis (submitted by manufacturer).—Total solids 5.20%, moisture 94.8%, ash 0.4%, fat 0.1%, protein 1.5%, available carbohydrates (total sugar as invert) 1.5%, crude fiber 0.4%, carbohydrates other than crude fiber (by difference) 2.8% and sodium 70 parts per million.

Calories.—0.13 per gram; 3.7 per ounce.

Use.—For use in calory-restricted diets.

DIET-DELIGHT BRAND SPINACH consists of the vegetable itself, packed in water without any added salt.

Analysis (submitted by manufacturer).—Total solids 6.70%, moisture 93.3%, ash 1.2%, fat 0.5%, protein 2.1%, crude fiber 0.6%, available carbohydrates (total sugar as invert) 0.7%, carbohydrates other than crude fiber (by difference) 2.3% and sodium 215 parts per million.

Calories.—0.16 per gram; 4.5 per ounce.

Use.—For use in calory-restricted diets.

Council on Physical Medicine and Rehabilitation

REPORT OF THE COUNCIL

The Council on Physical Medicine and Rehabilitation has authorized publication of the following report.

HOWARD A. CARTER, *Secretary.*

HOME WHIRLPOOL AERATOR ACCEPTED

Manufacturer: Home Physical Therapy Equipment Co., 141 East 56th Street, New York 22.

The Home Whirlpool Aerator is a device consisting of pipe, fittings, a venturi and a dial thermometer, designed to replace the ornamental spout on a bathtub or basin in the home and intended to agitate and aerate the water so as to give the patient the benefit of a whirlpool bath at any desired temperature up to that of the hot water supply. There are no electrical connections, home water pressure supplying the power for agitation and aeration on the same principle as that of the common laboratory water-driven aspirating pump. The air is drawn in through a perpendicular air pipe open at the upper end. The weight of the entire device is 2.3 Kg. (5 lb.), and it is 51 cm. (20¼ in.) in length. The shipping weight is 4 Kg. (9 lb.). Evidence was obtained from sources acceptable to the Council indicating that this device was well made and worked as claimed by the manufacturer. The Council on Physical Medicine and Rehabilitation voted to include the Home Whirlpool Aerator in its list of accepted devices.

Home Whirlpool Aerator

TRIPPE DIAPHRAGM INTRODUCER ACCEPTED

Manufacturer: Trippe Products Company, Hartsdale, N. Y.

The Trippe Diaphragm Introducer is a device intended to facilitate the insertion of vaginal diaphragms for contraceptive purposes. It is 21 cm. (8½ in.) in length, has a swivel tip at one end to facilitate releasing of the diaphragm and a hook at the other end to facilitate removal of the diaphragm, and makes a package weighing 40 Gm. (1⅓ oz.). The Council on Physical Medicine and Rehabilitation voted to include the Trippe Diaphragm Introducer in its list of accepted devices.

NATIONAL HEARING AID, VANITY MODEL 506, ACCEPTED

Manufacturer: National Hearing Aid Laboratories, 815 South Hill Street, Los Angeles 14.

The National Hearing Aid, Vanity Model 506, is an electric device recommended for the rehabilitation of the hard-of-hearing. With the exclusion of the clothing clips at the side, the case measures 129 by 60 by 24 mm. (tapering to 20 mm.). The weight of the case alone is 111.5 Gm. With the batteries, receiver cord and receiver, it weighs 195.5 Gm. The Council's test showed that electro-acoustic measurements, material, construction and performance were as reported by the manufacturer. The Council on Physical Medicine and Rehabilitation voted to include the National Hearing Aid, Vanity Model 506, in its list of accepted devices.

National Hearing Aid, Vanity Model 506

MAICO QUIET-EAR HEARING AIDS, MODELS G AND H, ACCEPTED

Manufacturer: The Maico Company, Inc., 21 North Third Street, Minneapolis 1.

The Maico Quiet-Ear Hearing Aids, Models G and H, are electric devices of conventional shape and arrangement; each measures 60 by 22 mm. in width and thickness. They differ, however, in length and weight. Model G measures 111 mm.; Model H, 99 mm. The transmitter unit of Model G weighs 119 Gm.; that of Model H, 122 Gm. Model G has a slightly higher battery drain and a correspondingly higher acoustic gain. The Council's investigation showed that the electro-acoustic properties, material construction and performance were as represented by the manufacturer. The Council on Physical Medicine and Rehabilitation voted to include the Maico Quiet-Ear Hearing Aids, Models G and H, in its list of accepted devices.

Maico Quiet-Ear Hearing Aid, Models G & H

GLOLITE LUMINOUS INFRARED RAY LAMPS, MODELS 439, 751, 1151 AND 1451, ACCEPTED

Manufacturer: Paul E. Johnson Manufacturers, Inc., 2508 South Parkway, Chicago 16.

The Glolite Luminous Infrared Ray Lamps emit both visible and infrared radiation in the range from 7,000 to 80,000 angstroms for therapeutic purposes. All four lamps are floorstand models and require a source of either direct or alternating current at 110 to 120 volts. Model 439 has a 450 watt heating element. Models 751, 1151 and 1451 require 660, 1,100 and 1,450 watts, respectively. The source of radiation for all lamps is made of resistance wire embedded in a non-metallic substance. The dimensions and weights are as follows:

Model	439	751	1151	1451
Weight				
unpacked, Kg.....	6.5	16.2	18	23.5
unpacked, lb.....	14.5	36	40	52
shipping, domestic, Kg.	8.5	19.5	21.5	27.5
shipping, domestic, lb..	19	43	47	61
shipping, foreign, Kg.	14.5	29	31	39.5
shipping, foreign, lb..	32	64	68	88
Height				
unpacked, cm.....	143	170	182	187
unpacked, in.....	57.5	68	73	75

Glolite Luminous Infrared Ray Lamp

Evidence from sources acceptable to the Council indicated that these lamps are satisfactory generators of radiant heat for therapeutic purposes. The Council on Physical Medicine and Rehabilitation voted to include the Glolite Luminous Infrared Ray Lamps, Models 439, 751, 1151 and 1451, in its list of accepted devices.

MICROTONE "CLASSIC" HEARING AID, MODEL T9, ACCEPTED

Manufacturer: The Microtone Company, Ford Parkway on the Mississippi, St. Paul 1.

The Microtone "Classic" Hearing Aid, Model T9, is a conventional electric hearing aid. For operation it requires a 1.5 volt A-battery and a 15 volt B-battery, both of the zinc-carbon type. With batteries it weighs 164.7 Gm. The external dimensions, excluding the clips, are 78 by 56 by 20 mm. Tubes, microphone, volume control and sealed amplifier unit are all removable. Evidence from acceptable sources as to electro-acoustic properties and clinical performance showed that this instrument was satisfactory. The Council on Physical Medicine and Rehabilitation voted to include the Microtone "Classic" Hearing Aid, Model T9, in its list of accepted devices.

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SATURDAY, NOVEMBER 25, 1950

LET'S KEEP AMERICA HEALTHY

A Guest Editorial

JOHN EDGAR HOOVER
Director, Federal Bureau of Investigation, United States Department of Justice

The life of a nation, in many respects, is similar to the life of an individual. A nation is born, grows in strength, is beset by ills and, unless properly cared for, may succumb to a fatal disease. Like an individual, a nation, in order to survive, must be healthy: physically, intellectually and spiritually. However, though human life, physically speaking, must have an end, a nation, kept strong, virile and healthy by the combined efforts of its citizens, can have life forever.

America, in this mid-twentieth century year, is a strong nation, great in material possessions and rich in spiritual resources. Born amid turmoil, a mere infant among the great powers of Europe, it possessed sturdy tissues, strong muscles and a sound heart. The founding fathers, in laying the foundations of America, planned well. The concepts of democracy, free government and the dignity of the individual were the beacon lights, the compasses of direction, guiding the paths of Americans toward the magnificent achievements of the next century and a half. Freedom of speech, religion and the press, embedded in a government of law, was the matrix in which we developed. America grew quickly from an infant into a bounding youngster and today into the mature responsibilities of adulthood.

But today the germs of an alien ideology, Communism, are attempting to infect the blood stream of American life—and to destroy the America we love and cherish. These Communist germs, spawned in the swamps of iniquity and terror, have blotted out, for one third of the world's population, the sunshine of free thought, independent research and unfettered inquiry. They have "sickened" many nations and literally killed countless persons. These germs are infectious and deadly, easily transmitted and often difficult to detect. This is America's task today, if we are to survive as a nation: to kill these Communist germs and to increase the strength and vigor of American resistance. In other words we must make democracy ever more workable, mature and worth while.

The physicians of America, by the very nature of their training, can render inestimable services in this ideological fight. Medical science is interested in cause and effect, in careful diagnosis, detection of specific symptoms and the prescribing of cures which will eliminate the cause of the malady. Physicians realize the value — in fact, the essential need — of clinical inquiry, unhampered by preconceived prejudices and suppositions; the calm appraisal of facts, and the absolute requirement that injuries and sicknesses be treated by professional, competent hands, not by amateurs and the inexperienced. Hysteria, impulsive actions and decisions not based on all the facts may mean disaster.

The fight against Communism must be waged, if we are to win, on the same principles which have enabled the medical profession to render such magnificent services for the American people. Communism is not something mystifying, impenetrable or impervious to observation. Not at all. Communism, despite its philosophical trappings and double talk veneer, can be analyzed. Through the stethoscope of observation and study, we can learn "what makes it tick." Communism means deceit, hypocrisy and duplicity, the glorification of force and violence, the destruction of liberty and freedom, the triumph of the state over the individual, the enthronement of falsehood, injustice, inequality and terror as the accepted standards of conduct. These are the central themes of Marxism-Leninism; the heartbeats of an atheistic philosophy which denies the spiritual basis of man's existence on earth. If these principles conquer the world, Western civilization—the way of life which has made possible the achievements of America — will be obliterated. The Communists, within minutes, would expunge 2,500 years of human history.

Americans, having learned the true inner meaning of Marxism-Leninism, will be alert to the hypocrisy of Communist siren calls. They will realize that when a Communist speaks of "peace," he really means "war," that when he poses as a champion of "free government" he, in fact, means the dictatorship of a ruthless minority. Communists are disloyal to our democracy; their allegiance is to Moscow. They would siphon away the free spirit of America, destroy the concepts of 1776 and establish a Soviet America—to become an "outpost" for Russian imperialism.

The FBI is the governmental agency designated to protect the internal security of the United States. The President in a directive dated July 24, 1950, called on all law enforcement agencies, patriotic organizations and individuals to report any information coming to their attention concerning espionage, sabotage and subversive activities to the FBI. The FBI, as the investigative arm of the United States Department of Justice, is a fact-finding agency. Our task is to obtain the facts,

completely, accurately and impartially. The physicians of America, like other citizens, can best help in the protection of the nation's internal security by reporting immediately to the FBI any information of this nature which might come into their possession. The FBI is not interested in opinions or ideas, idle rumor or malicious gossip—only in facts. Like you, as physicians, we want to know the unvarnished facts of the case. To fulfil our responsibilities, we seek to determine all available facts and then forward them without comment or evaluation to the Department of Justice. The FBI is not a policy-making agency. It does not decide whether there will, or will not, be prosecution. That decision rests exclusively with the Attorney General and his assistants.

Americans can defeat the Communist challenge—and in a democratic manner. Witch hunts, hysteria and vigilante actions are repugnant to the democratic tradition. They weaken the majesty of law and provide the Communist agitators with additional talking points. If each person in America would stop and think, learn to "peel off" the "outer skin" of Communism, often deceptively painted with glittering promises and glorious utopias, and recognize Communism for what it is—terror and injustice—then America would have no fear.

The keys of victory must be alertness, eternal vigilance and the maintenance of calmness. A healthy nation, like a healthy body, must receive the unstinting cooperation of all its component parts; if one part fails to carry its share the whole organism is weakened. America, at this critical hour, must remain strong and healthy. This is the task of each and every person.

MEDICAL EDUCATION IN TIME OF NATIONAL EMERGENCY

The statement of the Joint Committee on Medical Education in Time of National Emergency which appears on page 1111 of this issue, presents the recommendations of the Association of American Medical Colleges and the Council on Medical Education and Hospitals with respect to the conduct of medical education in the present national emergency and its possible sequelae. This statement has been submitted to the Health Resources Advisory Committee to the National Security Resources Board and to the National Advisory Committee on the Selection of Doctors, Dentists and Allied Specialists to the Selective Service System. These committees have been assigned major responsibilities by the President and the Congress for planning and regulating the mobilization and utilization of medical manpower in the present emergency.

The aim of the Joint Committee's statement is to emphasize the importance to the health, safety and interest of both the armed forces and the civilian population of a continuing flow of well trained physicians and to point out that to provide such a flow the quality of medical education must be vigilantly guarded. The statement also points out that of parallel importance is the continued training of graduate students in the basic sciences to provide the personnel trained in these fields so urgently needed to staff the preclinical departments of the medical schools and for the continuation of basic research in the medical sciences.

The statement makes recommendations on the handling of a number of specific problems, including the maintenance of an adequate supply of preprofessional students, the obligation of medical students to serve their country after completion of training, the broadening of the medical curriculum to meet the special medical problems that accompany a national emergency, the need for an increase in the production of physicians, the faculty requirements of the medical schools and the importance of maintaining a strong program for the training of residents.

Because experience has shown that such a program produces immature and incompletely trained physicians, the Joint Committee specifically recommends against the adoption of an accelerated program of the type employed in World War II. Adherence to such a program over a prolonged period would have an unquestioned deleterious effect on the quality of the medical schools. Since these schools constitute in truth a vital national resource, their integrity must be preserved as a matter of national interest. Instead of the accelerated program, the Joint Committee recommends that the academic year be extended in all schools to provide the additional training that will be needed by physicians to meet the special problems occurring in time of national emergency. Thus, an extension of the academic year would make it possible to give more training in such subjects as the prevention and treatment of radiation injuries, bacteriologic warfare, chemical warfare, civilian disaster relief, public health, preventive medicine, and epidemiology in relation to disaster areas, traumatic medicine and surgery, industrial medicine and rehabilitation and utilization of manpower.

On the basis of the experience with the AST and V-12 programs in World War II, the Joint Committee also recommends against placing medical students in uniform or having them subsidized as a group by the government. Instead it recommends that consideration be given to a program of government scholarships to be awarded on the basis of economic need and demonstrated academic superiority to students recommended by the medical schools. The committee also recommends that there be consideration of a program of government loans for students needing such assistance.

The statement of the Joint Committee has been carefully and thoughtfully prepared after conferences extending over more than four months with medical educators, representatives of government agencies and representatives of the medical profession. Of much help were the extensive studies made after the end of

World War II by the Committee on Preparedness for War of the Association of American Medical Colleges. This statement presents the carefully weighed thoughts of outstanding medical educators and should receive the serious consideration that it deserves.

MIDCENTURY WHITE HOUSE CONFERENCE

Concern for the health and welfare of children is an old American habit. The repetition of this concern by the decennial White House Conferences has now become a custom. At approximately 10 year intervals since President Theodore Roosevelt called the first conference in 1909 to plan for the care of dependent children, the president in office has gathered together the leaders in health, welfare and education to take stock of current practices and lay plans for further improvement of the children of the nation.

Among the many recommendations of the first White House Conference was the creation of a Children's Bureau. This Children's Bureau, created in 1912, gave leadership to the second White House Conference in 1919 under President Woodrow Wilson, as the closing activity of the "Children's Year." This conference was concerned essentially with child welfare standards and the health of children and mothers. Though many of its recommended child welfare laws and child health practices were controversial, those with merit have survived.

President Herbert Hoover called the third White House Conference on Child Health and Protection in 1930 to study the "present status of the health and well-being of the children of the United States . . . to report what is being done, and to recommend what ought to be done and how to do it." This third conference widened the range so that all children were included, not only those who were dependent or handicapped.

The 1940 White House Conference on Children in a Democracy was called by President Franklin D. Roosevelt. It was much broader in scope than any of the others, considering for the first time economic resources, religion, housing, play and recreation, as well as health, social welfare and education. One of the outcomes was the impetus given to the programs for handicapped children.

The Midcentury White House Conference on Children and Youth, to be held in December 1950, "bases its concern for children on the primacy of spiritual values, democratic practice and the dignity and worth of every individual. Accordingly, the purpose of the conference shall be to consider how the mental, emotional, and spiritual qualities essential to individual happiness and responsible citizenship can be developed in children and what physical, economic, and social conditions are deemed necessary to this development."

It is apparent that the Midcentury White House Conference will attempt to organize all the information available on what influences healthy personality development and, on the basis of this information, point the way to better organized mental hygiene activities. Qualified persons concerned with the home, the church, the school, health service, social service, recreation, employment and a number of other activities will pool their information and discuss ways to plan proper guidance during childhood and adolescence.

Physicians are interested in the physical and emotional problems of children. They should, therefore, be vitally interested in the deliberations of the Midcentury White House Conference. Physician delegates will have an opportunity to influence the thinking of the people of the United States on how best to accomplish this important objective of healthy personality development.

The fact that the Midcentury White House Conference is held when there exists a sharp controversy over compulsory health insurance should not prevent physician delegates from participating in the conference and contributing to its development. White House Conferences have become an American tradition. They are held each 10 years irrespective of the party in power and have been generally constructive. Physicians should actively participate in the conference to promote constructive results and prevent political manipulation.

MATERNAL DEATHS—ONE IN A THOUSAND

THE JOURNAL takes pride in announcing that for the first time in history the maternal mortality rate for a large nation—the United States of America—has been pushed slightly below the apparently irreducible minimum of 1 maternal death per 1,000 live births. When the 1949 rates for Sweden, Norway, Denmark, the Netherlands and New Zealand become available, one or more of these small countries with homogeneous populations may join the United States in the select group of countries with maternal mortality rates of 1.0 or less. The 1933 rates for the United States, Sweden and (the whites of) New Zealand were 6.2, 3.1 and 4.4. Reductions in maternal mortality in the United States are, however, remarkable because they have been made in a population which contains, as a result of immigration, many diverse groups from the health standpoint. According to compilations of the number of maternal deaths and live births in the several states by the Bureau of Medical Economic Research of the American Medical Association, the provisional 1949 maternal mortality rate for the entire United States —counting all maternal deaths among all classes and groups in the entire country—was closer to 1.0 than to 0.9 on the basis of the fifth revision of the Manual of the International List of Causes of Death (1938). Some of the state and city health departments used the fifth and others used the sixth revision (1948) of the International List in coding the causes of deaths in 1949. Hence, the "true" national

maternal mortality rate for 1949, a transition year in coding the causes of death, may never be known. The 1948 rate was 1.2.

Rarely has THE JOURNAL had the opportunity to call to the attention of the world in such definite terms the extraordinary accomplishments of the American medical profession, aided and abetted by auxiliary personnel and unequaled hospital facilities. But it is more than a story of tremendous medical progress. The fact that the chances of an expectant mother surviving the diseases of pregnancy, childbirth and the puerperium are now better than 999 out of 1,000 is truly a story of human and social progress.

This great record in maternal care takes the medical historian back to the days of Semmelweis in Austria, who led the medical profession toward the ideal of extreme cleanliness in maternity cases—the true pioneer of antisepsis in obstetrics. Previously, Oliver Wendell Holmes had pointed out the contagiousness of puerperal fever. One also thinks of Lister, a pioneer in antisepsis. It also takes one back to the late 1920's and early 1930's—when many of the soldiers, sailors and marines now fighting in Korea were born—when the maternal death rate was seven times as high as in 1949.

This glorious achievement of medical progress has not been limited to the wealthier states with almost exclusively white populations. In 1949 there were 30 states with rates less than 1.0, two at exactly that level and only 17 above. The highest state rate of 2.3 in 1949 for Mississippi was only one half of the lowest state rate, 4.3, in 1933. An examination of the rates for the different states indicates areas in which further improvement can be expected, but it is clear that maternal mortality is no longer a nationwide problem. Of course, it will be more difficult to maintain an extremely low level as the rate approaches even closer to 0.

What accounts for this phenomenal reduction in maternal mortality from 6.2 in 1933—the first year in which all of the states were in both the death and birth registration areas—to less than 1.0 in 1949? The increasing percentage of births in hospitals is an important factor, although improvements in the medical care provided in home births have been pronounced. A second factor is the development of a concept of prenatal care which stresses early diagnosis of some of the conditions which formerly contributed to death. Health education, particularly that given by the public health nurse in prenatal care, has aided greatly. In many cities the maternal health program of the local health department has been effective in reducing maternal mortality. In the actual treatment of complications, the basic factors in the last decade and a half have been the administration of sulfonamides, antibiotics and whole blood or blood derivatives. But steady improvement in undergraduate and postgraduate medical training in obstetrics is the most important factor in welding together these other forces. Unlike the trend in many nations, the number of births attended by midwives in the United States is being rapidly reduced. For a number of years many state and county medical societies have had special committees which review every maternal death in their areas and use their findings as a basis for improving all aspects of prenatal, intranatal and postnatal care. These study groups of organized medicine have been a tremendous factor in preventing maternal deaths and in producing phenomenally low maternal mortality rates.

This is, indeed, a story of human as well as medical progress. The fact that the chances of survival for the mother are better than 999 out of 1,000 should bring comfort and consolation in a troubled era to expectant mothers and their husbands, their children and their parents. Childbearing has been made quite safe.

SPECIALTY JOURNALS OF THE AMERICAN MEDICAL ASSOCIATION

The October numbers of the nine specialty journals of the American Medical Association were published with a number of changes which are intended to identify them more closely with the Association and to help meet certain problems facing these journals. The titles of the publications have been changed to include the designation "A. M. A." as part of the title, so that the new titles appear as, for example, *A. M. A. Archives of Surgery* and *A. M. A. Archives of Internal Medicine.* This change was undertaken after consideration by the chief editors of the journals and their editorial boards and the Board of Trustees.

The primary purpose of the use of the letters A. M. A. is to effect a closer identification of these journals with the American Medical Association in the minds of the readers and others who learn of the journals. Although the explanatory statement "Published monthly by the American Medical Association" appears on the bottom of the cover page, there has been some misunderstanding concerning the sponsorship of these journals. The periodicals are now identified in much the same way as other allied specialty journals are identified with the organization that sponsors them. Consideration was given to the use of the full name of the Association as, for example, "American Medical Association Surgery" and "American Medical Association Archives of Surgery." However, after consultation with librarians, book publishers and others, it was concluded that it was preferable to use the identifying symbol A. M. A.

Concurrently with the change in title, the color of the cover was changed to white with the titles being identified in different colors. An attempt was made to select a color for the title that would match the former color of the cover. This change also was made to indicate the close relation of the specialty journals. In addition, it

was believed that there would be an improvement in the appearance—which has been borne out by the comments from other publishers—and permit use of this space for advertising purposes. While the specialty journals are not intended to be a source of profit for the American Medical Association, costs of labor and paper, to mention just two items, have increased so much in the past two years that various means had to be sought to meet in part these increased expenditures. The table of contents, which formerly was found on the back cover page, has been moved to the pages immediately preceding the first article or editorial.

These changes were announced to subscribers through a special statement in the September number of each of the journals, and a reference to the change was made in the report of the Board of Trustees in the Oct. 21, 1950, issue of THE JOURNAL. Several inquiries have arisen from libraries regarding the cataloging or indexing of the journals with the new titles. Beginning with volume 49 (January-June, 1951) the *Quarterly Cumulative Index Medicus* will list these journals under the new titles, so that the letters A. M. A. will be considered as an integral part of the titles. For the completion of volume 48 (July-December, 1950) the *Quarterly Cumulative Index Medicus* will continue to use the old titles without the designation A. M. A. The changes were made before the current volume numbers were completed because of certain production difficulties which required a number of changes in October.

ORIGIN OF THE BILE PIGMENTS

One of the most widely accepted statements in basic science medical literature is that the bile pigments are derived from the breakdown of blood hemoglobin. The evidence for this view dates back at least 100 years to the now classic observation of Virchow [1] that the orange pigment, "hematoidin," found at the site of old blood extravasations were similar to bilirubin. Many years later, Hans Fischer and his co-workers [2] conclusively demonstrated that "hematoidin" was identical with bilirubin. Other well known investigators who contributed evidence in support of the above view include Kühne, Herrmann and, more recently in this country, Whipple and his group,[3] who demonstrated that the heme of hemoglobin is almost quantitatively converted to bilirubin in the dog.

Currently, the problem of the origin of the bile pigments is being reinvestigated at Columbia University with the modern isotopic tracer technic. These studies in general confirm the earlier classic view that the bile pigments are derived from destroyed hemoglobin of red cells. Hematin which had been previously "labeled" with isotopic N^{15}, by the administration of glycine containing N^{15}, was found to be readily converted to bile pigment in the dog.[4] The isolated bile pigments were found to contain the isotopic N^{15} derived from the administered hematin. Similar results were obtained in normal human subjects.[5] However, the additional rather unexpected observation was made that at least 11 per cent of the bile pigment was derived from sources other than the breakdown of hemoglobin. The normal male subjects were given glycine containing N^{15}. Previous work by this group of investigators has demonstrated that the glycine is incorporated into the heme portion of the hemoglobin molecule. Furthermore, these investigators had shown that the labeled hemoglobin remains in the circulating erythrocytes for approximately 120 days, until the red cell is destroyed. Thus, if bile pigment is derived solely from hemoglobin liberated from destroyed erythrocytes, then no significant amount of N^{15} should be found in the bile pigment until nearly 120 days after the administration of N^{15} labeled glycine. Actually, a prompt and pronounced rise in N^{15} containing bile pigment (stercobilin isolated from the feces) was found. A second, expected rise approximately 100 to 140 days after the administration of the N^{15} glycine was observed. Undoubtedly the labeled bile pigment in this case was derived from the destroyed N^{15} labeled hemoglobin. The early rise in labeled bile pigment was even more pronounced in patients with pernicious anemia [6] and with congenital porphyria.[7] A large part, at least 31 per cent, of the bile pigment, stercobilin, obtained from stools of the latter patient was formed from sources other than the hemoglobin of the mature erythrocyte.

The nature of the unknown precursor of bile pigments has not yet been determined. Several possibilities have been suggested.[5] The "extra" bile pigment may be derived from hemoglobin which has escaped incorporation into erythrocytes, or from myoglobin as suggested years ago by Whipple,[8] or from the cytochromes or catalase, or from porphyrins or heme not utilized for hemoglobin synthesis or perhaps from a direct synthesis of bile pigment not involving the porphyrins. The solution of this problem should add considerably to the understanding of the origin and metabolism of the bile pigments. Thus it appears today that the long-established view that the bile pigments are derived solely from the breakdown of hemoglobin must now be modified to include other, as yet unidentified, probably nonhemoglobin, precursors in normal man and particularly in patients with pernicious anemia and congenital porphyria.

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WASHINGTON NEWS

(From the Washington Office of the American Medical Association)

The New Congress

The *Congressional Quarterly*, a legislative information service, concludes that the administration will have six fewer supporters for its domestic policy in the new Senate. Eight senators-elect are listed as certain to oppose Mr. Truman's chief domestic proposals: Richard Nixon (Republican, California), George A. Smathers (Democrat, Florida), Herman Welker (Republican, Idaho), Frank Carlson (Republican, Kansas), Willis Smith (Democrat, North Carolina), James Duff (Republican, Pennsylvania) and Wallace F. Bennett (Republican, Utah). The net loss is expected to be reduced to six because of support for Mr. Truman from Thomas C. Hennings (Democrat, Missouri) and A. S. (Mike) Monroney (Democrat, Oklahoma).

Twenty-three Democratic first-termers elected in 1948 (all mid-westerners) were among that party's 28 House casualities. . . . The Congress actually will not be very "new"; about 85 per cent of the membership served previously in the House or Senate, including 18 out of office during the Eighty-First Congress. . . . Defeat of Representative Vito Marcantonio (American Labor Party, New York) means no minor party representative for the first time in 40 years. . . . Frazier Reams of Ohio, a long time Democrat who won as an Independent, will vote with Democrats on organizing the House, but says he will "remain aloof" from the party. . . . Southerners, as usual, dominate committee chairmanships, with eleven. Incidentally, committee chairmen average six years younger, 60 instead of the 68 of the Eighty-First Congress. . . . Even so, chairmen will average seven years older than the average age for both houses, about 53. . . . Representative Robert L. Doughton (Democrat, North Carolina) continues to hold his title as the oldest member, 87, while the youngest will be reelected Representative Lloyd M. Bentsen Jr. (Democrat, Texas), who will be 29 the day Congress opens. . . . There will be no change among House leaders, but a major reshuffling of Senate leadership will be required because of election defeats. . . . Of the nine representatives who tried for the Senate, four were successful; of five who tried for governor, two lost.

The Present Session of Congress

Theoretically, the present session opening next week could turn its attention to the long list of health bills not passed in the last two years. But practically, this is impossible. Extension of rent controls, new taxes, revision of the antisubversive bill, Alaskan and Hawaiian statehood, defense and other top priority bills should keep House and Senate occupied until time for adjournment in December. When this Congress passes out of existence, it will take with it such unfinished medical legislation as aid to medical education, aid to local public health units, aid to school health programs, national compulsory health insurance and the various plans to stimulate voluntary insurance. However, one can expect to see all these bills come to life again in the new Congress after the first of the year.

Military Notes

Although the Army as a whole has not been able to put into effect the "point system" for release of reserves, its medical department is more fortunate. A spokesman said the Surgeon General's office in most cases still expects to release World War II medical reserves from active duty when they have completed necessary training and when replacements are available. With a steady supply of physicians assured by the doctor-draft, the medical department at the present time is not experiencing the same manpower difficulties as are other branches. But, as usual, it will not be possible to apply the release policy in every case. . . . Deane W. Malott, president of the National Association of State Universities and Association of Land-Grant Colleges, spoke against the proposal to defer high-ranking students in all courses. He advocated that all men be required to serve 18 months to two years at a time of their choice between the ages of 18 and 26. This, he pointed out, would give the military services a variety of professionally trained and skilled men and would lessen the chance of good students rushing to "easy" courses where their grades would be higher. . . . Endorsing a recommendation of Dr. Howard A. Rusk's Committee on Veterans Hospitals, VA Medical Director Dr. Paul B. Magnuson points out that VA has the facilities and beds to care for many of the Defense Department's wounded returned from overseas but that there has been no request for use of these facilities. He mentioned care for amputees, artificial limb service, training and rehabilitation and plastic surgery as specific fields where VA is thoroughly equipped to care for patients. In the absence of a system for transferring patients, he says military services are wasting medical manpower. . . . In another speech recently Dr. Magnuson urged voluntary workers to help VA get rehabilitated men to leave VA hospitals. He warned against turning VA hospitals into "country clubs," where men tend to stay longer than necessary, denying others hospital care.

Deferment of Interns and Residents

In an effort to insure the deferment of interns and residents who are essential to the community welfare in their present positions, Dr. Howard A. Rusk has sent special instructions to state chairmen of voluntary advisory committees. Dr. Rusk, chairman of the National Advisory Committee to Selective Service, emphasized that evidence of essentiality must be presented to the registrant's local board, which is not necessarily located in the same community as the hospital. He asked state chairmen and local committees to "support fully" before local boards any claims of essentiality which may be presented in behalf of a registrant whose hospital is located elsewhere.

Public Health Service Needs Doctors

The Public Health Service, faced with civil defense as well as overseas responsibilities, is finding difficulty in recruiting professional personnel. Although the service has campaigned constantly for physicians, it was able to add only 30 commissioned medical officers to its rolls between July 1 and mid-October. The totals are 1,038 and 1,068. In addition, the Public Health Service has 114 full time Civil Service physicians and 150 part time. The Division of International Health (PHS) at present is attempting to sign up 15 qualified physicians for the ECA program in Indochina, Thailand, Burma and Indonesia. In these areas emphasis will be placed on the prevention and control of tropical diseases. The Public Health Service is in immediate need of three physicians to serve with its mission to Liberia, which operates under State Department funds and also carries on preventive and control activities. In Greece, the Public Health Service has conducted a program for three years, concentrating on hospital rehabilitation, water supply installations, tuberculosis control and nurse training. At least 100 physicians will be needed for foreign service in the next year, when a number of new programs will be set up. Under consideration are projects for Turkey, Iran, Formosa and the Philippines. Although base pay for commissioned officers ranges from $4,500 to $5,500 per year, various allowances more than double the total income. Civil Service appointments carry

salaries of $6,400 to $8,800, with 25 per cent additional allowed for service in Southeast Asia and quarters allowances that vary from $2,000 to $2,400.

The Public Health Service is scheduling examinations for assistant surgeons and senior assistant surgeons in the PHS Regular Corps. Examinations will be held throughout the country on Feb. 12, 13 and 14, 1951, but applications must be in by January 15. Applications and information may be obtained from the Surgeon General, U. S. Public Health Service, Federal Security Agency, Washington 25, D. C., Attention: Division of Commissioned Officers.

Survey of Health Services

Directors of the special congressional survey of health services say that information is coming in at a satisfactory pace, but they are not able to say whether a complete report will be ready by next February 1, the deadline set by the Senate Labor and Public Welfare Committee. The survey, to cover state and local health facilities as well as voluntary plans, is being handled by a committee under the chairmanship of Dr. Dean Clark. Blue Cross and Blue Shield organizations expect to turn in information on their operations by December 1, as do commercial insurance companies. Additional data will be supplied on medical plans operated by such nonprofit organizations as cooperatives and labor unions, and A.M.A.'s Chicago headquarters will gather details on medically sponsored programs not under Blue Shield.

Stockpile of Medical Supplies

The federal government again has come under criticism from a New York state official for delay in setting up medical stockpiles under the civil defense program. In approving allocation of $500,000 in state funds for this purpose, Governor Thomas E. Dewey said, "Apparently the federal government not only has no plans but no intention of providing medical supplies, and these, of course, are of first importance." A few weeks ago similar views were expressed by Dr. Herman Hilleboe, New York health officer. In reply, a National Security Resources Board spokesman points out that this agency has neither money nor authority to start regional reserves of medical supplies and equipment. New York and NSRB representatives are expected to meet soon in an effort to reach some agreement on respective responsibilities. Governor Dewey said supplies to be purchased by the state will be mainly drugs and antibiotics, blood transfusion sets, burn and treatment supplies, fracture supplies, syringes and needles and surgical kits.

Food and Drug Administration Convictions

The Food and Drug Administration's report on convictions for October deviates from its usual prosaic style to tell how agents tracked down two herb doctors in the hills of Oklahoma and in Memphis, Tenn. In the first case a Food and Drug inspector visited the "Indian herb doctor" in Oklahoma as a "patient." After looking at the agent's hands and nails, the "doctor" diagnosed the ailment as "sugar diabetes" and prescribed a concoction three times a week. In line of duty the inspector had to gulp down a glass of the stuff. Re-orders of the herbs (in fruit jars with the patient's name the only label) were delivered by "runners," who crossed state lines in private cars. The "Indian herb doctor" was permanently enjoined against interstate shipping and labeling of his wares.

The second case, the "African herb doctor" from Memphis, fined $9,000 and given nine years in prison, concerns a West African who prepares herbs from a book by Dr. Culpepper, an English physician who died in 1640. The "African herb doctor" was not a stranger to the law. Previously, he had been convicted in Michigan, Arkansas and Tennessee for illegal practice of medicine, served a jail term for mail fraud and had signed a Federal Trade Commission stipulation in 1943 to the effect that a hair-growing formula was ineffective. This time he was convicted on 15 counts for shipping four herbal medicines misbranded with false claims.

Elsewhere, 10 druggists were convicted for selling barbiturates and other potent drugs without prescription. There were several other cases of misbranding and shipping faulty products.

Notes

Two new National Advisory Councils, authorized by the last session of Congress, have been set up within the National Institutes of Health. At the time it announced members of the new councils (Arthritis and Metabolic Diseases and Neurological Diseases and Blindness) NIH also announced names of new members appointed to existing councils. Eighteen of the 43 new appointments go to physicians.

Members of the National Advisory Arthritis, Rheumatism and Metabolic Diseases Council are William P. Holbrook, M.D., Tucson, Ariz.; Clyde E. Wildman, president, De Pauw University, Greencastle, Ind.; Weston Howland, head New England chapter of Arthritis and Rheumatism Foundation, Milton, Mass.; C. James Watson, M.D., chairman, Department of Medicine, University of Minnesota, Minneapolis; Philip S. Hench, M.D., chief, Department of Rheumatic Diseases, Mayo Clinic; Floyd B. Odlum, business executive, New York City; Richard H. Freyberg, M.D., associate professor of clinical medicine, Cornell Medical College, New York City; Maxwell M. Wintrobe, M.D., head, Department of Internal Medicine, University of Utah, Salt Lake City, and John A. Reed, M.D., clinical professor of medicine, George Washington University Medical School, Washington, D. C.

Members of the National Advisory Neurological Diseases and Blindness Council are Percival Bailey, M.D., professor of neurology and neurological surgery, University of Illinois Medical College, Chicago; Cecil A. Johnson, lawyer, Chicago; Henry W. Woltman, M.D., chairman, Neurology and Psychiatry sections, Mayo Foundation Graduate School; George Baehr, M.D., professor and director of clinical research, Columbia University; Leonard Goldenson, New York; Dan Gordon, M.D., assistant professor of clinical surgery, Cornell Medical College, New York City; H. Houston Merritt, M.D., director, Neurology Institute, Presbyterian Hospital, New York City; Cornelius H. Traeger, M.D., head, National Society for Multiple Sclerosis, New York; Dilworth W. Woolley, Rockefeller Institute, New York; J. S. Ulmer, lawyer, Cleveland; P. F. Lucchesi, M.D., professor of pediatrics, Temple Medical School, Philadelphia, and W. Kuhn Barnett, educator, Richmond, Va.

Other newly appointed physicians are Robert F. Loeb, recently appointed to the National Science Foundation and professor at Columbia University—appointed to the National Advisory Health Council; Irvine H. Page, director, Cleveland Clinic Foundation, and member of the National Research Council, and Hugh J. Morgan, physician and chief of Vanderbilt University Hospital, Nashville—appointed to the National Advisory Heart Council. William Malamud, professor and head, Department of Psychiatry, Boston University Medical School, and Samuel B. Wortis, director, Psychiatry and Neurological Service, Bellevue Medical Center, New York University—appointed to the National Advisory Mental Health Council.

Each advisory council meets for one or two days quarterly to review applications for grants and make recommendations to the Surgeon General as to which grants should be issued. Grants are previously screened by NIH, but the councils set the priority of grants and the amount to be spent. These grant programs now total about $50,000,000 per year, compared with about $4,000,000 in 1946. Members of the councils meet together once a year to discuss interrelated programs of the various divisions of NIH. They receive $50 per diem while actually engaged in council work but no salary.

GOVERNMENT SERVICES

Army

New Type of Army Medical Company

A preventive medicine unit of company size, first of several of its kind now being organized by the Army Medical Service, has arrived in the Far East Command for duty in Korea, Major Gen. R. W. Bliss, the Surgeon General, has announced.

Successor to the malaria survey and malaria control detachments of World War II, the new company has functions beyond the scope of previous units of this type. In addition to malaria control and survey, the units will be responsible for inspections of field sanitary conditions and control of insect-borne, waterborne and other diseases. When acting in support of combat troops, these companies will operate as far forward as necessary to accomplish their mission.

The new preventive medicine companies are composed of six officers, one warrant officer and 59 enlisted men. Units are being organized at Brooke Army Medical Center, Fort Sam Houston, Texas. Officer personnel are qualified entomologists or sanitary engineers and the enlisted men have had training in one or more phases of preventive medicine. The preventive medicine company is composed of a headquarters section, to accomplish command and administrative work, and a preventive medicine service subdivided into a hygiene and sanitation section, survey section and three control sections.

The hygiene and sanitation section investigates water points, waste disposal, troop shelter, bathing and laundering facilities, mess sanitation, contamination of food or water and adequacy of clothing. The survey section inspects sanitary discipline in other units, determines the incidence and distribution of insect-borne and similar diseases and checks on the origin of cases of these diseases admitted to hospitals in its area. The control section furnishes technical supervision for work details engaged in sanitary control measures, conducts on-the-job training of soldiers in insect and rodent control measures and recommends corrective measures for other units.

Public Health Service

Regular Corps Examination for Medical Officers

An examination for appointment of medical officers in the Regular Corps of the Public Health Service will be held Feb. 12-14, 1951, at points throughout the United States. Applications must be received no later than Jan. 15, 1951. Appointments will be made in the grades of assistant surgeon (equivalent to Navy rank of lieutenant [j.g.]) and senior assistant surgeon (equivalent to lieutenant). Appointments are permanent in nature and provide opportunities to qualified physicians for a career in clinical medicine, research and public health. Applicants who successfully complete this examination may ordinarily expect appointment as soon as they become eligible.

The requirements for both grades are United States citizenship, at least 21 years of age, graduation from a recognized school of medicine and, for assistant surgeon, at least seven years of educational training and professional experience subsequent to high school. For senior assistant surgeon, at least 10 years of educational training and professional experience subsequent to high school are required. Physicians who are successful in the examination and are now serving internships will not be placed on active duty in the Regular Corps until completion of internship.

The examination will include an oral interview, physical examination and written objective tests covering the professional field. The written professional examination for the grade of assistant surgeon will cover basic medical sciences, internal medicine (including neurology and psychiatry), therapeutics and toxicology, pediatrics, and medical problems of obstetrics and gynecology, surgery, orthopedics, gynecology, obstetric procedures, and preventive medicine and public health. The examination for senior assistant surgeon will include the above subjects with the exception of anatomy.

Physical requirements: Candidates must be physically qualified as a result of an examination performed at a Public Health Service facility; it is recommended that applicants complete this examination as soon as possible to obviate the necessity of taking the written examination if found not physically qualified. Candidates who have a physical defect, or who have had serious illness or injury, should attach a statement to their applications outlining in detail the nature of such illnesses or injuries, treatment received, periods of hospitalization, length of absence from work and present status.

Entrance pay for an assistant surgeon with dependents is $5,686.56 per annum, and for senior assistant surgeon with dependents, $6,546. These figures include the $1,200 annual additional pay received by medical officers as well as subsistence and rental allowance. Officers on active duty are not eligible to receive disability compensation from the Veterans Administration. Retirement pay after 30 years of service or at the age of 64 is three-fourths annual basic pay at the time of retirement. Retirement for disability is authorized. Additional benefits include periodic pay increases (time served as a member of the armed forces is credited), 30 days' annual leave, sick leave, full medical care and the usual privileges extended to officers of the military forces. Information may be obtained from the Surgeon General, United States Public Health Service, Washington 25, D. C. Attention: Division of Commissioned Officers.

Air Force

Director of Research

Col. Paul A. Campbell, who recently gave up private practice in Chicago to accept a regular commission in the air force, has returned to the Air Force School of Aviation Medicine, Randolph Air Force Base, Texas, as director of research. For many years he specialized in otolaryngology, which he taught at Rush Medical College, the University of Illinois and Northwestern medical schools. He made his first solo flight 10 years ago. He is program chairman for the Aero Medical Association, has served as medical consultant for United Airlines, senior attending staff surgeon for Wesley Memorial Hospital, Chicago, and consultant for the Air Force Surgeon General. Colonel Campbell has published many technical papers and has written chapters for medical textbooks. He served in Europe during World War II. His decorations include the Legion of Merit, the Army Commendation Medal and the Royal Order of the Sword of Sweden.

Personal

Col. Robert J. Platt, former surgeon of the Far Eastern Air Force, has been named commandant of the Alabama branch of the Air Force School of Aviation Medicine. The new branch of the Air Force medical school will be located at Gunter Air Force Base, Montgomery, Ala., where all flight nurse and airman training will be conducted. Colonel Platt is a 1927 honor graduate of the School of Aviation Medicine.

MEDICAL NEWS

(Physicians will confer a favor by sending for this department items of news of general interest: such as relate to society activities, new hospitals, education and public health. Programs should be received at least two weeks before the date of meeting.)

ARIZONA

Mental Health Program.—A meeting to activate the newly formed Arizona Association for Mental Health was held November 13 in Phoenix. The organization first came into being at planning sessions held in Phoenix last August 3, when Arizona became the thirty-fourth state to organize a citizen's mental health association.

Further aid in developing a mental health program for the state was made recently by three mothers' clubs of Nogales, which sent a check to the state treasurer to deposit to the account of a special mental health fund for Arizona.

CALIFORNIA

Personal.—Dr. Eugene M. Farber has been promoted to the director of the Division of Dermatology and associate professor of dermatology (medicine) at Stanford University School of Medicine, San Francisco. He is also chief of dermatology at Stanford University Hospitals, San Francisco.

Hospital News.—The new unit of Mount Zion Hospital, San Francisco, which was opened in November, provides over 150 additional beds, making a new total of 325 for the entire hospital. The Harold Brunn Institute for Cardiovascular Research will occupy about 7,000 square feet, in association with cancer and tuberculosis research carried on by staff members.

Basic Science Courses.—St. Mary's Hospital in San Francisco will present basic science courses in applied anatomy and physiology and biochemistry throughout the year. The anatomy lectures are being presented by Dr. Harold H. Lindner, lecturer in anatomy and clinical assistant in surgery at the University of California Medical School, Berkeley-San Francisco. These lectures are being given on Thursdays from 7:45 p. m. to 9:15 p. m. There will be no lecture the week of Thanksgiving. Subjects of lectures beginning November 30 and for the succeeding weeks through February include the tongue, cervical nerve tracts, prevertebral area of the neck, cervical vertebrae, the axilla, female breast, thoracic wall, mediastinum, lungs and pleura and anterior abdominal wall. The biochemistry and physiology lectures are being given on alternating Saturdays from 9:00 to 10:00 a. m. by Harold A. Harper, Ph.D., lecturer in surgery at the University of California School of Medicine, San Francisco, and director of the chemistry laboratory of the hospital. Beginning with the November 25 lecture, the subjects will be physiology of the kidney, physiological and chemical aspects of shock, physiological basis of liver function tests, enzymes in tissue metabolism and carbohydrate metabolism.

IDAHO

State Association Committees Appointed.—The Idaho State Medical Association's Armed Forces Advisory Committee was elected by members of the component society committees at a meeting in Boise October 21. Dr. Orval F. Swindell, Boise, former president of the association and secretary-treasurer of the Welfare and Grievance Committee, was named chairman. Other members are Drs. Clifford O. Armstrong, Moscow; Fred A. Pittenger, Boise; Charles A. Terhune, Burley, and Harvey E. Guyett, Idaho Falls. Dr. Verne J. Reynolds, Boise, has been appointed chairman of the association's Civilian Defense Committee. Other members include Drs. Judson B. Morris, Boise; Lester L. Shupe, Caldwell; Henry C. Turner, Pocatello; Dauchy Migel, Idaho Falls; Fred T. Kolouch, Twin Falls; James W. Hawkins, Coeur d'Alene; Robert E. Staley, Kellogg, and James H. Bauman, Lewiston.

ILLINOIS

Lake Pollution Suit Ending.—Dismissal of the last defendants in the suit brought by the State of Illinois seven years ago against the State of Indiana and 24 of its cities and industries to compel a halt on Lake Michigan pollution has been recommended to the United States Supreme Court. All the defendents, it is reported, have complied with the court's requirements at a cost of nearly $15,000,000. Pollution was a threat to the metropolitan water supply and recreational areas caused by Indiana's dumping of raw sewage and untreated industrial wastes into Lake Michigan and streams emptying into it. The original suit was filed by the Illinois Attorney General Oct. 9, 1943 against Indiana and the cities of Gary, Hammond, East Chicago and Whiting, and in 1945 twenty industries were added as co-defendants. Thereafter lawyers for both sides stipulated antipollution measures that, when completed, would allow the defendants to be dropped from the suit.

Chicago

Chicago Medical Society.—Two guest speakers will address the Chicago Medical Society at its meeting December 13 at 8:00 p. m. in the John B. Murphy Memorial Auditorium. Dr. Perrin H. Long, Baltimore, will speak on "Current Clinical Usage of Antibiotics," and Comdr. Thomas J. Canty (MC, USN), Oakland, Calif., on "Amputation Surgery and Recent Developments in Artificial Limbs."

Institute of Medicine Annual Meeting.—Dr. Stanley Gibson, professor of pediatrics emeritus, Northwestern University Medical School, will deliver the presidential address at the thirty-fifth annual meeting of the Institute of Medicine of Chicago December 5 at the Furniture Club of America. His subject will be "Diagnosis of Congenital Cardiovascular Anomalies Amenable to Surgery."

Ophthalmological Society Prize.—The Chicago Ophthalmological Society announces that friends of the late Dr. Louis Bothman have contributed money through his medical fraternity, Phi Delta Epsilon, for a yearly prize of $100 for the best paper submitted to the society by an ophthalmologist who has completed his training within the previous six years. Such paper may be used as an entrance thesis for membership in the society. Papers for the first award should be submitted to the secretary of the society, Dr. Gail R. Soper, 636 Church Street, Evanston, Ill., not later than July 1, 1951.

INDIANA

Monthly Series of Telephone Seminars.—The Indiana University School of Medicine, with the cooperation of the Indiana State Medical Association, has scheduled a monthly series of telephone seminars in postgraduate medical education, which will be carried by leased wires to gatherings of physicians throughout the state. The first of these was presented November 7. Success of a test program from the auditorium of the medical school by closed telephone circuit to a meeting of the St. Elizabeth hospital staff in Lafayette led to endorsement of the program by the medical school council and the committee on medical education of the state association. Fifteen county societies listened in on the program. This method permits the local doctors of the county to attend these meetings without the necessity of long and hazardous driving in winter months and also makes it possible for speakers to make their comments without unnecessary driving. The flexibility of this plan makes the most outstanding experts in all fields of medical science available to the entire profession of Indiana. To enable listeners to receive the full value from the telephone program there will soon be available to each physician a listing in a brochure carrying a picture of the speaker with a biographical sketch, an outline of his remarks, together with any reproductions of illustrations or charts he might normally use in his presentation. It is hoped that before long every county society within the state will be participating in the program.

KENTUCKY

Exhibit Wins Award.—A silver award from the American Roentgen Ray Society was given to an exhibit presented by the department of radiology at Veterans Administration Hospital and the University of Louisville School of Medicine. The exhibit on abdominal aortography showed new uses and possibilities in the technic. Dr. David Shapiro, chief radiologist at the hospital and assistant professor of radiology at the medical school, and Drs. Joseph C. Bell, Everett L. Pirkey, and Gerald M. Peterson, physicians on the faculty of the medical school, prepared the display.

MASSACHUSETTS

Tufts Alumni Lecture.—The annual medical alumni lecture will be given by Dr. Frederick W. Maroney, Brooklyn College, New York, December 5 at 8:00 p. m. at the Tufts College Medical School, Boston, on "Protect the Power House." This lecture is given annually by a distinguished alumnus of the medical school who is not on its faculty. Physicians, students and the faculty of Tufts College Medical School are invited.

Clinical Anesthesiology.—A new program in clinical anesthesiology is being offered by Boston University School of Medicine under Dr. Julia G. Arrowood, professor of anesthesiology. The course is designed for physicians practicing anesthesia in community hospitals. Clinical facilities for the course have been made available at Massachusetts Memorial Hospitals. Students are admitted as full time members of the resident staff for three months. They are guided in preoperative and postoperative care of the patient, as well as in administering anesthesia for clinical surgery. They participate in clinics and conferences and may prepare for examinations of the American Board of Anesthesiology. No fees are required. Clinical facilities limit the enrolment to two students at a time.

MICHIGAN

State Medical Election.—The newly elected officers of the Michigan State Medical Society are Dr. Clarence E. Umphrey, Detroit, president; Dr. Otto O. Beck, Birmingham, president-elect; Dr. L. Fernald Foster, Bay City, secretary, and Dr. Andrew S. Brunk, Detroit, treasurer.

Public Health Conference.—The thirtieth annual Michigan Public Health Conference will be held in the Pantlind Hotel and Civic Auditorium, Grand Rapids, November 29-December 1 to consider "New Weapons in the Battle Against Disease" and the role of public health personnel in civil defense and in time of disaster. Physicians interested are cordially invited to attend the conference sessions. Copies of the program may be obtained from the Michigan Department of Health, Lansing.

MINNESOTA

Personal.—The Republic of Syria has sent to Dr. Khalil G. Wakim, Rochester, the medal of highest order of merit in appreciation of his services to the medical school of the National University of Syria in Damascus. At the request of the Syrian government Dr. Wakim was sent by the State Department in Washington to give lectures and help reorganize the medical school.

Course in Obstetrics.—A continuation course in obstetrics for general physicians will be presented at the University of Minnesota, Minneapolis, December 15 and 16. Visiting faculty members for the course will include Dr. Emil G. Holmstrom, University of Utah School of Medicine, Salt Lake City; Dr. Curtis J. Lund, Louisiana State University School of Medicine, New Orleans, and Dr. Charles E. McLennan, Stanford University School of Medicine, San Francisco.

NEBRASKA

Carey Memorial Lecture.—The third annual Dr. Eben J. Carey Memorial Lecture will be delivered November 27 at 8:00 p. m. in the Joslyn Memorial Art Museum Lecture Hall at Omaha by Dr. C. Rollins Hanlon, head of the department of surgery, St. Louis University School of Medicine, on "Surgical Treatment of Cardiovascular Disease." This lecture is sponsored by Creighton University and the Phi Chi Medical Fraternity. Previously Dr. Hanlon was associate professor of surgery at Johns Hopkins University. Preceding the lecture Dr. Hanlon will be entertained at a dinner at the Omaha Athletic Club by the Phi Chi Medical Fraternity. Dr. Carey, in whose memory these lectures are given, was at the time of his death dean of the Marquette University School of Medicine, Milwaukee. For many years he had held a national office in the Phi Chi Medical Fraternity.

NEW YORK

Allergy Society Lecture.—Dr. Carl E. Arbesman, instructor in bacteriology and immunology, University of Buffalo School of Medicine, will speak on "Testing and Newer Therapy in Asthma and Hay Fever" at a meeting of the Allergy Society of Syracuse November 29 at 8:30 p. m. at University Hospital. The lecture has been arranged by the Medical Society of the State of New York in cooperation with the New York State Department of Health.

Incidence of Cerebral Palsy.—The number of persons handicapped by cerebral palsy annually is more than twice the number who are moderately or severely handicapped as a result of poliomyelitis, according to Dr. I. Jay Brightman, Albany, assistant commissioner for medical services of the New York State Department of Health. He told the meeting of the New York State Association for Crippled Children that cerebral palsy occurs in about six patients in every 1,000 births, which in New York means 1,500 new cases per year. Of these, 100 have minor involvement and 200 die early in life. Thus the total of cerebral palsied added to the population is 1,200 or more. It was reported that New York City will open two classes for cerebral palsied in Public School 85, the Bronx, and plans are under way for a similar unit on Staten Island.

Academy Programs.—The Rochester Academy of Medicine has arranged the following programs for its Tuesday evening (8:30) monthly meetings:

Dec. 5, D. Gordon Murray, Toronto, Canada, Surgery of Congenital Heart Disease.
Jan. 9, Joe W. Howland, Rochester, N. Y., moderator, Symposium on Medical Problems in Atomic Energy.
Feb. 6, Hugh McCulloch, Chicago, Recent Advances in Rheumatic Fever.
March 6, Philip S. Hench, Rochester, Minn., Uses of ACTH.
April 3, Edith H. Quimby, Sc.D., New York, Clinical Uses of Radioactive Isotopes.

New York City

Panel on Pulmonary Tuberculosis.—The Tuberculosis Sanatorium Conference of Metropolitan New York will hold its clinical session on chronic pulmonary disease November 29 at 8:15 p. m. in the Cornell University Medical College Amphitheatre. There will be a panel discussion on the "Correlation of Pathological, Clinical and Roentgenologic Findings in Patients with Pulmonary Tuberculosis Having Lung Resection."

Infant Mortality Committee Program.—The special committee on infant mortality of the Medical Society of the County of New York is continuing its monthly meetings open to all members of the medical and nursing profession and medical students. Meetings are held in the Academy of Medicine Building the first Wednesday of each month at 8:30 p. m. At the first meeting, November 1, Dr. Louis M. Hellman, Baltimore, spoke on "Prevention of Prematurity." The next five lectures are:

Dec. 6, Priscilla White, Boston, Treatment of the Diabetic Mother and Her Newborn Child.
Jan. 3, Rustin McIntosh, New York, The Pediatrician's Responsibility to the Newborn During the First Seven Days of Life.
Feb. 7, Bronson Crothers, Boston, Neurological Problems of the Neonatal Period.
March 7, R. Gordon Douglas, New York, and Charles A. Weymuller, Brooklyn, Obstetrical Anesthesia and Analgesia as It Affects Neonatal Mortality.
April 4, Edith L. Potter, Chicago, Atelectasis in the Newborn.

Expand School Health Service.—School health services have been extended to five additional academic high schools as part of the city health department's work. The department now gives school health services in 18 academic high schools with a school population of 56,000 and 31 vocational high schools with 45,000 pupils, in addition to the services which it has long given in the elementary parochial and public schools. Services are given in 646 elementary public schools with a registration of 665,000 and 340 elementary parochial schools with 230,000 pupils. During the 1949-1950 school year the department of health conducted 6,005 doctor sessions in the high schools and nurses spent 47,117 nursing hours at work in high schools. The department also conducted 39,008 examinations of pupils in its general health supervision work; of that number 20,653 required further follow-up and study. During the year 25,138 students were referred to school physicians or nurses because of either illness or accidental injury. Private physicians examined and reported on 16,089 students; of these 2,535 required further follow-up study and care.

OHIO

Dr. Derryberry Receives Prentiss Award.—C. Mayhew Derryberry, Ph.D. chief, division of public health education, U. S. Public Health Service, was awarded the Elisabeth Severance Prentiss National Award in Health Education at the tenth anniversary civic luncheon of the Cleveland Health Museum November 13. Given annually since 1944 by the Cleveland Health Museum, the award serves a dual purpose: (1) to honor the memory of the museum's first foundation benefactress and (2) to encourage, through recognition, outstanding work in the field of health. Dr. Derryberry is one of the early proponents of new types of discussion technics. Under his leadership the Health Education Section, U. S. Public Health Service, has become a strong administrative unit. He was associate director of research, American Child Health Association, 1933-1935; research assistant, New York University, 1932-1936, and since 1936 has been with the Public Health Service. He has been devoted to improvement of technics of health education. Previous recipients of the award were Dr. Harry E. Kleinschmidt, retired master craftsman in health education mediums, 1949; Dr. Donald B. Armstrong, Metropolitan Life Insurance Co., 1948;

Dr. W. W. Bauer, American Medical Association, 1947; Mary P. Connolly, University of Michigan, 1946; Charles E. A. Winslow, Ph.D., Yale University, 1945, and Mary S. and Evart G. Routzahn, Russell Sage Foundation, 1944.

PENNSYLVANIA

Benjamin Rush Awards.—The Medical Society of the State of Pennsylvania presented these awards during its one hundredth annual session in October in Philadelphia. Leroy Mikels of Stroudsburg, Monroe County, was selected as "the outstanding lay individual who contributed most to the advancement of public health and to the improvement of health conditions in his respective community" during the past year. The Trexler Foundation of Allentown, Lehigh County, received the award as "the outstanding lay organization of Pennsylvania which did most to advance public health and to improve health conditions in the area it serves" during the past year. The winning counties' nominees were among 34 selected by the 22 component societies for the state awards.

Mr. Mikel financed, and guided through the depression years of the thirties, Monroe County's first bedside nursing service. During the past year the Red Cross Public Health Nursing Service, organized and financially helped by him, made 18,000 visits to Monroe County families. He organized in 1949 the voluntary public Blood Donor Program, which provides free blood and plasma to county residents. He was chairman of the American Red Cross Chapter in the Poconos from 1929 to 1947.

The Trexler Foundation, established in 1934, is a privately endowed organization that yearly allocates about $250,000 "for the support of community health organizations and programs, for recreational facilities that support health, and for youth agencies that teach and encourage healthful living and good citizenship" within Allentown and Lehigh County.

Philadelphia

Hospital Residents Banquet.—The sixty-fourth annual banquet of the Association of Ex-Resident and Resident Physicians of the Philadelphia General Hospital will be held December 5 at 7:00 p. m. at the Penn-Sheraton Hotel. Reservations may be had by writing to the secretary-treasurer: Dr. Robert C. McElroy, Room 514, 133 South Thirty-Sixth Street, Philadelphia 4.

Hospital Begins 40 Hour Week.—All employees, including 54 nurses and the century-old Woman's Medical College of Pennsylvania and its hospital, went on a 40 hour week beginning November 13. It is the first hospital in the city to adopt the standard industrial work week across the board. In some cases, particularly among nursing personnel, the new policy means a reduction in weekly work hours of as much as 17 per cent. More than 200 employees are affected. The step was taken, said a spokesman for the college and hospital, mainly to halt the siphoning of skilled employees into industry and business and thus to cut down expensive and crippling turnover in jobs.

GENERAL

Rockefeller Resigns as Institute Head.—John D. Rockefeller Jr. has resigned as president of the Board of Trustees of the Rockefeller Institute for Medical Research and was succeeded by his youngest son, David. Mr. Rockefeller will continue as a member of the board, with which he has been associated since its founding by his father in 1901. David Rockefeller is director of the Carnegie Endowment for International Peace, second vice president of the Chase National Bank and a trustee of the University of Chicago.

Society Election.—At the meeting of the International Union Against Tuberculosis, which was held in Copenhagen, Denmark, September 3-6, Prof. K. A. Jensen of Copenhagen assumed office as president; Dr. Manoel de Abreu of Rio de Janeiro was made president-elect; Prof. Etienne Bernard of Paris was reelected secretary-general, and M. Mirabaud of Paris was elected treasurer. The Twelfth Conference of the International Union Against Tuberculosis will be held in Rio de Janeiro in July or August 1952.

Plastic Surgeons Meeting in Mexico.—The American Society of Plastic and Reconstructive Surgery will hold its annual meeting at the Hotel Del Prado, México, D. F., November 26-29, under the presidency of Dr. Leon E. Sutton, Syracuse, N. Y. The society has been invited to attend the meetings of the Plastic Surgery Section of the IX Asamblea Nacional de Cirujanos, which has arranged preconvention activities. Dr. G. Sanvenero-Roselli, Milan, Italy, has been invited to speak. His subject will be "Congenital Malformations of the Face."

Harriman to Head Red Cross.—E. Roland Harriman, vice chairman of the board of governors, has been appointed by President Truman to succeed General George C. Marshall as president of the American Red Cross December 1. Mr. Harriman was chairman of a committee that planned the reorganization of the Red Cross and was manager of the organization's North Atlantic area during the war. He is also chairman of the Board of Directors of the Union Pacific Railroad. General Marshall was appointed president of the Red Cross on Sept. 22, 1949 and has continued to serve in that capacity since his recent appointment as defense secretary.

Markle Foundation Report.—The John and Mary R. Markle Foundation granted more than $800,000 to medical schools and other educational institutions in the year ending June 30, according to the annual report released in October. Of the grants, $500,000 went to medical colleges in the United States and Canada to help young faculty members become established in academic medicine, part of a five year program to build up teaching and research staffs of the schools. Twenty medical schools received $25,000 each for this purpose. Other grants included $110,000 to the Association of American Medical Colleges for research in medical education, $100,000 to the Social Science Research Council and a like amount to the American Council of Learned Societies.

Western Surgical Association.—This association will hold its annual meeting November 29 to December 2 at the Radisson Hotel in Minneapolis under the presidency of Dr. Warren H. Cole, Chicago. Invited speakers include:

Robert P. Meyer, Robert W. Ehrlich, C. Bruce Taylor and John M. Dorsey, Chicago, Experimental Bronchotracheal Anastomosis.
Thomas C. Douglass, W. Harrison Mehn, Benjamin F. Lounsbury, LaVern L. Swigart and Carlos Tanturi, Chicago, Attempts at Experimental Production of Portal Hypertension.
Donald E. Preshaw, Alfred M. Large and Arthur F. Johnson, Detroit, Effect of Portacaval Venous Shunt on Sulfobromophthalein Retention.
Charles S. Rife, Milwaukee, Benign Duodenal Colic Fistula.
Harold Laufman, Frederick W. Preston and Robert V. Bourdeau, Chicago, Efficacy of Hemostatic Agents in the Presence of Anticoagulant Therapy.
Walter R. Stager, Omaha, Bloodshed Conservation and Autotransfusion.

The annual dinner will be held December 1 after a cocktail hour at 6:30 p. m.

Radiological Society Meeting.—The Radiological Society of North America, Inc., will hold its annual meeting December 10-15 at the Palmer House, Chicago, under the presidency of Dr. Warren W. Furey, Chicago. Those presenting papers by invitation include:

Bronson S. Ray, Howard S. Dunbar and Charles T. Dotter, New York, Dural Sinus Venography.
Joseph Hanelin and William R. Eyler, Boston, Pulmonary Artery Thrombosis: Roentgen Manifestations.
Russell Wigh and Frederick R. Gilmore, Philadelphia, Solitary Pulmonary Necrosis: Comparison of Neoplastic and Inflammatory Conditions.
Janet E. Towne and Charles J. Smith, Chicago, Indications for Surgical Intervention in Carcinoma of the Cervix.
Dallas B. Phemister, Chicago, Multiple and Solitary Infarction of Bone in Adults.
Joseph B. Kirsner and Walter L. Palmer, Chicago, Reversibility in Ulcerative Colitis; Clinical and Roentgenologic Observations.
Joseph L. Morton, George W. Callendine, M.S., William G. Meyers, Ph.D., Columbus, Ohio, The Co^{60} Nylon Thread, a New Interstitial Radiation Therapy.
Herbert C. Allen Jr., Raymond L. Libby, Ph.D., Benedict Cassen, Ph.D., Los Angeles, The Scintillation Counter in Clinical Studies of Human Thyroid Physiology Using I^{131}.
George E. Moore and Richard B. Bridenbaugh, Minneapolis, Roentgen Demonstration of the Venous Circulation in the Liver Portal Venography.
Charles B. Huggins and E. V. Jensen, Ph.D., Chicago, Plasma Proteins in Cancer.

A series of refresher courses will be presented beginning with two on Sunday and seven courses daily from 8:30 to 10 a. m. Nonmembers will be charged a fee for the courses. Both scientific and commercial exhibits will be shown. The Carman Lecture will be given Tuesday evening at 8:00 p. m. by Dr. Furey on "The Development of Cardiovascular Radiology." The annual banquet will be held Thursday at 7 p. m.

Prevalence of Whooping Cough.—According to the U. S. Public Health Service, although the week ended November 11 is near the seasonal low week for whooping cough, more new cases of this disease were reported than any other of the common diseases of childhood. A total of 1,780 cases was reported as compared with 1,504 for the same week in 1949, and the 5-year median was 1,863 cases. The cumulative total since the seasonal low week, which falls between September 27 and October 3, is 9,374 as compared with 8,657 for 1949. The cumulative total for the "disease" year 1949-50 which ended September 30 was 118,731, which is more than double the total for the previous year, when 56,635 cases were reported. Estimated mortality rates based on a 10 per cent sample of deaths for the first 8 months of 1950 was 0.8 per 100,000 population, which was 60 per cent higher than that for a similar period in 1949.

AAAS Cleveland Meeting.—The annual meeting of the American Association for the Advancement of Science will be held in Cleveland December 26-30. All 17 of the association's sections and subsections and about 40 scientific societies will hold more than 200 sessions in the Public Auditorium and downtown hotels—Statler, Hollenden, Carter and Allerton. Programs of particular interest to those in the fields of medicine and experimental biology include:

Section C—Chemistry. Two, of the 12 sessions, on steroid hormones, December 28, a. m. and p. m.; one on medicinal chemistry, evening of December 29.

Subsection Nm—Medicine. Four-session symposium on Biological Effects of Radiation, December 29 and 30, a. m. and p. m.

Subsection Np—Pharmacy, jointly with the American Pharmaceutical Association, Scientific Session, December 28 and 29.

Information may be obtained from Dr. R. L. Taylor, Assistant Administrative Secretary, AAAS, 1515 Massachusetts Ave., N. W., Washington, D. C.

LATIN AMERICA

Postgraduate Short Course in Cuba.—This course will be presented December 4-6 at the Liceo de Camaguey under the auspices of the Colegio Médico de Camaguey and the Sociedad de Estudios Médicos y Quirurgicos de Camaguey. It will consist of medical lectures given in English and translated into Spanish, lantern slides and discussions. John Elliot, Sc.D., and Dr. Carlos A. P. Lamar, Miami Fla.; Drs. Robert B. Greenblatt, Augusta, Ga.; E. Perry McCullagh, Cleveland, and Henry H. Turner, Oklahoma City, will be the lecturers. Their subjects will be endocrine problems in childhood, diagnosis and treatment; testicular dysfunction; ovarian dysfunction; blood transfusion; metabolism of carbohydrates; Selye's syndrome of alarm; shock; thyroid disorders; toxic hyperthyroidism treatment; cortical hyperadrenalism; Rh factor; cancer of the breast; hormonal treatment; syndrome of pale large ovaries; sexual maladjustment in married couples, diagnosis and treatment. Further information may be obtained from Colegio Médico de Camaguey, Camaguey, Cuba.

Medical Examinations and Licensure

COMING EXAMINATIONS AND MEETINGS

BOARDS OF MEDICAL EXAMINERS

ALABAMA: Montgomery, June 26-28. Sec., Dr. D. G. Gill, 519 Dexter Ave., Montgomery.

COLORADO: * Denver, Jan. 3-5, 1951. Exec. Sec., Mrs. B. M. Hudgens, 831 Republic Bldg., Denver.

DELAWARE: Dover, Jan. 9-11. *Reciprocity.* Jan. 18, 1951. Sec., Dr. J. S. McDaniel, 229 S. State St., Dover.

DISTRICT OF COLUMBIA:* *Reciprocity.* Washington, Dec. 11. Sec., Dr. Daniel L. Seckinger, 4130 E. Municipal Bldg., Washington.

FLORIDA: * Jacksonville, Nov. 26-28. Sec., Dr. Homer Pearson, 701 Dupont Bldg., Miami.

GEORGIA: Atlanta, June. Augusta, June. Sec., Mr. R. C. Coleman, 111 State Capitol, Atlanta.

GUAM: The Commission on Licensure will meet whenever a candidate appears or submits his credentials. Ex. Sec., Dr. John Y. Battenfield, Agana.

HAWAII: Honolulu, Jan. 8-11, 1951. Sec., Dr. I. L. Tilden, 1020 Kapiolani St., Honolulu.

IDAHO: Boise, Jan. 8, 1951. Sec., Mr. Armand L. Bird, 305 Sun Bldg., Boise.

ILLINOIS: Chicago, Jan. 9-11. Superintendent of Registration, Mr. Charles F. Kervin, Capitol Bldg., Springfield.

INDIANA: Indianapolis, June 20-22. Exec. Sec., Miss Ruth V. Kirk, 1138 K. of P. Bldg., Indianapolis 4.

IOWA: *Written.* Des Moines, Dec. 4-6. Acting Director, Dr. Walter L. Bierring, Division of Examination and Licensure, State Department of Health, 1027 Des Moines St., Des Moines.

KANSAS: Topeka, Dec. 13-14. Sec., Dr. O. W. Davidson, 772 New Brotherhood Bldg., Kansas City.

KENTUCKY: *Examination.* Louisville, Dec. 11-13. Sec., Dr. Bruce Underwood, 620 South Third St., Louisville.

LOUISIANA: New Orleans, Dec. 7-9. Sec., Dr. R. B. Harrison, 1507 Hibernia Bank Bldg., New Orleans.

MARYLAND: Baltimore, Dec 14-15. Sec., Dr. Lewis P. Gundry, 1215 Cathedral St., Baltimore 1. *Homeopathic.* Baltimore, Dec. 12-13. Sec., Dr. John A. Evans, 612 West 40th St., Baltimore.

MASSACHUSETTS: Boston, Jan. 23-26, 1951. Sec., Dr. Geo. R. Schadt, 17 State House, Boston.

MINNESOTA: * Minneapolis, Jan. 16-18. Sec., Dr. J. F. Du Bois, 230 Lowry Medical Arts Bldg., St. Paul 2.

MISSISSIPPI: Jackson, December. Asst. Sect., Dr. R. N. Whitfield, Jackson 113.

MONTANA: Helena, April 2-4. Sec., Dr. S. A. Cooney, 214 Power Block, Helena.

NEBRASKA:* June 1951. Director, Mr. Oscar F. Humble, Room 1009, State Capitol Bldg., Lincoln.

NEW HAMPSHIRE: *Examination.* Concord, March 14-15. Sec., Dr. John S. Wheeler, 107 State House, Concord.

NEW YORK: *Examination.* Albany, Buffalo, Syracuse and New York City, Jan. 30-Feb. 2. Sec., Dr. Jacob L. Lochner, 23 S. Pearl St., Albany.

NORTH CAROLINA: *Reciprocity.* Winston-Salem, Jan. 15. Sec., Dr. Joseph J. Combs, 419 Professional Bldg., Raleigh.

NORTH DAKOTA: Grand Forks, Jan. 3-6. Sec., Dr. C. J. Glaspel, Grafton.

OHIO: Columbus, December. Sec., Dr. H. M. Platter, 21 W. Broad St., Columbus.

OKLAHOMA:* *Examination.* Oklahoma City, June 6-7. Sec., Dr. Clinton Gallaher, 813 Braniff Bldg., Oklahoma City.

OREGON: * *Examination.* Portland, January 4-6. Sec., Mr. Howard I. Bobbit, 608 Failing Bldg., Portland 4.

PENNSYLVANIA: Philadelphia, January 1951. Acting Secretary, Mrs. M. G. Steiner, 351 Education Bldg., Harrisburg.

PUERTO RICO: *Examination.* Santurce, March 6. Sec., Mr. Luis Cueto Coll, Box 3717, Santurce.

RHODE ISLAND:* Providence, Jan. 4-5. Chief, Division of Profesional Regulation, Mr. Thomas B. Casey, 366 State Office Bldg., Providence.

SOUTH DAKOTA: * Jan. 15-16. Sioux Falls, South Dakota. Sec., Dr. C. E. Sherwood, 109 Center St., West, Madison.

TENNESSEE: * *Examination.*, Memphis, Dec. 21-22. Sec., Dr. H. W. Qualls, 1635 Exchange Bldg., Memphis 3.

UTAH: Salt Lake City, July 1951. Dir., Mr. Frank E. Lees, 324 State Capitol Bldg., Salt Lake City 1.

VERMONT: Burlington, February 1951. Sec., Dr. F. J. Lawliss, Richford.

VIRGINIA: Richmond, Nov. 30, Dec. 1-2. Sec., Dr. K. D. Graves, 631 First St., S.W., Roanoke.

WASHINGTON: * Seattle, January 1951. Sec., Mr. Edward C. Dohm, Department of Licenses, Olympia.

WEST VIRGINIA: Charleston, Jan. 8-10. Sec., Dr. N. H. Dyer, State Capitol, Charleston 5.

WISCONSIN: * River Falls, Jan. 9-11, 1951. Sec., Dr. C. A. Dawson, Tremont Bldg., River Falls.

WYOMING: *Examination.* Cheyenne, Feb. 5. Sec., Dr. Franklin D. Yoder, Capitol Bldg., Cheyenne.

BOARDS OF EXAMINERS IN THE BASIC SCIENCES

ARIZONA: *Examination.* Tucson, Dec. 19. Sec., Mr. Francis A. Roy, Room 423, University of Arizona, Tucson.

COLORADO: *Examination.* Denver, Dec. 6-7. Sec., Dr. Esther B. Starks, 1459 Ogden St., Denver 3.

CONNECTICUT: *Examination.* Feb. 10. Executive Asst., State Board of Healing Arts, Mr. M. G. Reynolds, 110 Whitney Ave., New Haven 10.

MICHIGAN: *Examination.* Detroit and Ann Arbor, Jan. 12-13. Sec., Miss Eloise LeBeau, 101 No. Walnut St., Lansing 13.

MINNESOTA: *Examination.* Minneapolis, Jan. 2-3. Sec., Dr. Raymond N. Bieter, 105 Millard Hall, University of Minnesota, Minneapolis.

NEBRASKA: *Examination.* Omaha, Jan. 9-10. Dir., Mr. Oscar F. Humble, Room 1009, State Capitol Bldg., Lincoln 9.

NEW MEXICO: *Examination.* Santa Fe, Dec. 10. Sec., Mrs. Marguerite Cantrell, P. O. Box 1522, Santa Fe.

OKLAHOMA: *Examination.* Oklahoma City, March 27. Sec., Dr. Clinton Gallaher, 813 Braniff Bldg., Oklahoma City.

OREGON: *Examination.* Portland, Dec. 2. Sec., Mr. Charles D. Byrne, State Board of Higher Education, Eugene.

SOUTH DAKOTA: Vermillion, Dec. 1-2. Sec., Dr. Gregg M. Evans, 310 E. 15th St., Yankton.

TENNESSEE: *Examination.* Memphis, Dec. 27-28. Sec., Dr. O. W. Hyman, 874 Union Avenue, Memphis.

WASHINGTON: Seattle, January 1951. Sec., Mr. Edward D. Dohm, Department of Licenses, Olympia.

WISCONSIN: *Examination.* Milwaukee, Dec. 2. Madison, April 7. Sec., Mr. W. H. Barber, Scott and Watson Sts., Ripon.

* Basic Science Certificate required.

Coming Medical Meetings

American Medical Association, Clinical Session, Cleveland, Dec. 5-8. Dr. George F. Lull, 535 N. Dearborn St., Chicago 10, Secretary.

American Academy of Dermatology and Syphilology, Palmer House, Chicago, Dec. 2-7. Dr. John E. Rauschkolb, P. O. Box 6565, Cleveland, Secretary.

American Association of Medical Clinics, Hotel Cleveland, Cleveland, Dec. 4. Dr. Arthur H. Griep, Welborn Clinic, Evansville, Ind., Secretary.

American Psychoanalytic Association, Waldorf-Astoria Hotel, New York, Dec. 7-10. Dr. LeRoy M. A. Maeder, 1910 Rittenhouse Square, Philadelphia 3, Secretary.

American Society of Plastic and Reconstructive Surgery, Mexico City, Mexico, Nov. 27-29. Dr. Clarence R. Straatsma, 66 E. 79th St., New York City, Secretary.

Puerto Rico, Medical Association of, Santurce, Dec. 13-17. Dr. Victor J. Montilla, P. O. Box 3866, Santurce 29, Secretary.

Radiological Society of North America, Palmer House, Chicago, Dec. 10-15. Dr. Donald S. Childs, 713 E. Genesee St., Syracuse 2, N. Y., Secretary.

Southern Surgical Association, Hollywood Beach Hotel, Hollywood, Fla., Dec. 5-7. Dr. John C. Burch, 2112 West End Ave., Nashville 5, Tenn., Secretary.

Western Surgical Association, Minneapolis, Nov. 30-Dec. 2. Dr. Michael Mason, 154 E. Erie St., Chicago, Secretary.

DEATHS

Kully, Herman Edward ● Omaha; born in Omaha Nov. 21, 1903; Creighton University School of Medicine, Omaha, 1929; assistant professor of otolaryngology and had been acting director of the department at his alma mater; specialist certified by the American Board of Otolaryngology; fellow of the American College of Surgeons; member of the American Academy of Ophthalmology and Otolaryngology; affiliated with Creighton Memorial St. Joseph's Hospital, Children's Memorial Hospital, Doctors Hospital, Lutheran Hospital and Douglas County Hospital; otolaryngological consultant for the Union Pacific Employees Hospital Association; died September 19, aged 46, of coronary thrombosis.

Norris, Samuel Royall, Jacksonville, Fla.; born in Raleigh, N. C., Feb. 7, 1897; University of Pennsylvania School of Medicine, Philadelphia, 1922; specialist certified by the American Board of Obstetrics and Gynecology; member of the American Medical Association; member and past president of the South Atlantic Association of Obstetricians and Gynecologists; past president of Duval County Medical Society; fellow of the American College of Surgeons; affiliated with St. Luke's, Riverside and Duval County hospitals; served during World War I; died September 21, aged 53, of lymphosarcoma.

Dalton, Richard Andrew Jr., Lafayette, La.; Louisiana State University School of Medicine, New Orleans, 1944; served as assistant surgeon in the U. S. Public Health Service Reserve and as a resident in internal medicine at the U. S. Marine Hospital in Staten Island, N. Y.; drowned while fishing at Grand Isle, August 5, aged 30.

Eudy, William Thomas, Eminence, Mo.; University of Louisville (Ky.) Medical Department, 1909; member of the American Medical Association; secretary of Carter-Shannon Counties Medical Society; served overseas during World War I; died in Poplar Bluff (Mo.) Hospital September 10, aged 75, of coronary heart disease.

Goodrich, Edson Everett, Rome, N. Y.; Baltimore University School of Medicine, 1900; served on the Mexican Border and overseas during World War I; for many years a physician to governmental branches in France; died September 9, aged 73.

Guntzer, Germaine Agatha, Honolulu, Hawaii; Cornell University Medical College, New York, 1931; died September 2, aged 50.

Johnson, Nimrod August, Santa Monica, Calif.; University of Minnesota College of Medicine and Surgery, Minneapolis, 1905; member of the Minnesota State Medical Association; fellow of the American College of Surgeons; formerly practiced in Minneapolis, where he was affiliated with Deaconess and St. Mary's hospitals; died in Minneapolis September 6, aged 69, of coronary thrombosis.

Lamb, Charles W., ● Forest Park, Ill.; Jenner Medical College, Chicago, 1910; died September 11, aged 71, of carcinoma of the tongue.

Miller, Albert Winters, Indianapolis; University of Indianapolis Medical Department, 1903; member of the American Medical Association; served as school physician; affiliated with St. Francis Hospital in Beech Grove; died September 12, aged 71, of cerebral hemorrhage.

Neergaard, Fred Adolph, Harriman, Tenn.; Maryland Medical College, Baltimore, 1908; member of the American Medical Association; past president of the Roane County Medical Society; formerly vice president of the Tennessee State Medical Association; served overseas during World War I; affiliated with Harriman Hospital; died in Kingston September 15, aged 67, of acute coronary occlusion.

Nelson, Francis Medard, Oakland, Calif.; Flint Medical College of New Orleans University, New Orleans, 1904; a medical examiner during World War I; Congressional medalist as examiner for Selective Service System during World War II; died September 6, aged 71, of cerebral accident.

Oman, Elmer Samuel, Columbus, Ohio; Ohio Medical University, Columbus, 1898; died September 13, aged 82, of cerebral hemorrhage.

Purnell, James D., Myrtle, Miss.; University of Tennessee Medical Department, Nashville, 1892; member of the American Medical Association; died in New Albany September 13, aged 82.

Ravdin, Marcus ● Evansville, Ind.; Memphis, (Tenn.) Hospital Medical College, 1900; an Associate Fellow of the American Medical Association; member of the American Academy of Ophthalmology and Otolaryngology; fellow of the American College of Surgeons; specialist certified by the American Board of Ophthalmology and American Board of Otolaryngology; consulting oculist Louisville and Nashville Railroad; on the staffs of St. Mary's Hospital and Deaconess Hospital, where he died September 12, aged 84, of heart disease.

Richey, Clifford Otto, Evansville, Ind.; Indiana University School of Medicine, Indianapolis, 1922; member of the American Medical Association; served during World Wars I and II; died in the Veterans Administration Hospital, Indianapolis, September 8, aged 51, of hypertensive cardiovascular disease.

Solley, Fred Palmer, New York; College of Physicians and Surgeons, medical department of Columbia College, New York, 1892; formerly on the faculty of his alma mater; past vice president of the New York Academy of Medicine; member of the American Medical Association; served on the staffs of the Knickerbocker Hospital, Presbyterian Hospital and St. Luke's Hospital, where he died September 7, aged 83, of aplastic anemia.

Spackman, Ross Hugh, New York; University of Toronto Faculty of Medicine, Toronto, Ont., Canada, 1928; member of the American Medical Association; served during World War II; died September 6, aged 48.

Spears, Tunis R., Washburn, Wis.; Rush Medical College, Chicago, 1889; health officer of Washburn; for many years physician for the Omaha Railway; died September 7, aged 87, of heart disease.

Speed, George William, Mullens, W. Va.; University of Cincinnati College of Medicine, 1935; member of the American Medical Association; served during World War II; affiliated with Mullens General Hospital; formerly on the staff of Madison (W. Va.) General Hospital; died in Raleigh General Hospital, Beckley, September 10, aged 42, of acute pancreatitis.

Squires, Frederick Eugene, Livonia, N. Y.; University of Buffalo School of Medicine, 1896; member of the American Medical Association; for many years town health officer; died in Strong Memorial Hospital, Rochester, September 13, aged 85.

Stein, Elias, Flushing, N. Y.; Long Island College of Medicine, Brooklyn, 1923; served during World War II; died October 4, aged 40, of heart disease.

Sterrett, William John, Pittsburgh; Western Pennsylvania Medical College, Pittsburgh, 1901; member of the American Medical Association; for many years trustee of Geneva College; veteran of the Spanish-American War; served on the Mexican border and during World War I; affiliated with Allegheny General Hospital, where he died September 5, aged 76.

Swayze, Henry Yandell, Center Point, Texas; Medical Department of Tulane University of Louisiana, New Orleans, 1893; fellow of the American College of Chest Physicians; served as superintendent of the Kerrville State Sanatorium in Kerrville; died August 30, aged 80, of heart failure.

Talbot, John ● Portland, Ore.; College of Physicians and Surgeons of San Francisco, 1916; died August 31, aged 73.

Taub, Israel Zangwill, New York; Northwestern University Medical School, Chicago, 1928; died in the Veterans Administration Hospital September 3, aged 57, of uremia.

Terry, Marcus Claude, Palo Alto, Calif.; Keokuk (Ia.) Medical College, 1897; Rush Medical College, Chicago, 1899; served during World War I; served on the staffs of various Veterans Administration hospitals; formerly clinical instructor of immunology at Leland Stanford Junior University School of Medicine; died in Salem, Ore., September 9, aged 79, of acute coronary occlusion.

Tinsley, Jack Byrd, Bethlehem, Pa.; Jefferson Medical College of Philadelphia, 1949; served during World War II; medical resident physician at St. Luke's Hospital, where he had been an intern and where he died September 6, aged 28, of lymphatism, blood transfusion reaction and secondary anemia.

Turner, Henry William Biddle ● Lieutenant Commander, U. S. Navy, retired, Miami, Fla.; University of Pennsylvania Department of Medicine, Philadelphia, 1906; entered the Medical Corps of the U. S. Navy as a lieutenant (jg) on July 30, 1908; placed on the retired list Nov. 1, 1930, after 22 years' naval service; died near Beaufort, S. C., August 3, aged 65, of injuries received in an automobile accident.

Utter, Henry Abraham, Harrisburg, Ill.; University of Arkansas School of Medicine, Little Rock, 1936; died August 19, aged 40, of heart disease.

● Indicates Fellow of the American Medical Association.

FOREIGN LETTERS

ITALY

(From a Regular Correspondent)

FLORENCE, Sept. 10, 1950.

Chronic Polyarthritis

Professor Rietti reported in a session of the Academy of Sciences of Ferrara his observations on 15 patients with primary chronic polyarthritis treated by the method of Lewin and Wassen. The method consists in the simultaneous injection of 5 mg. of desoxycorticosterone acetate intramuscularly and 1 Gm. of ascorbic acid intravenously. Results were favorable only in some cases. The speaker reported that this method is in conflict with experimental researches by Selye, but, from the theoretical and practical point of view, he believes that this therapeutic method should be tried on a large scale. It seems, in fact, that the desoxycorticosterone assumes properties similar to 17-hydroxy-11-dehydrocorticosterone (cortisone), a drug which at present is not at the disposal of the majority of the patients because of its high cost. In the discussion that followed, Professor Dogliotti confirmed, on the basis of personal experience, the good results obtainable with Lewin and Wassen's therapy in primary chronic arthritis. He expressed the opinion that success may be closely linked to a favorable quantitative relation between the doses of the two injected substances. Professor Aloisi advanced the hypothesis that the ascorbic acid acts on the desoxycorticosterone acetate by stimulating oxydation.

Electrophoresis and Chromatography in the Study of Protein

At the Superior Institute of Public Health, the Nobel prize winner Tiselius, professor of biochemistry of the University of Upsala, discussed electrophoresis and chromatography in the study of protein chemistry. He pointed out that, in the study of proteins and other substances of high molecular weight, the methods of fractioning and separation are of particular importance because they furnish fundamental indications which are necessary for chemical identification. Among the methods which have proved useful for this purpose is electrophoresis, which is based on the difference of migration of particles of substances under the influence of an electric current. Progress in this field of research was recently made with special apparatus for the continuous separation of large amounts of proteins and with the use of some ultramicromethods for the analysis of a drop of serum. Another method fairly useful for studying proteins is the analysis by adsorption or chromatography, developed by Tswett in 1906 and improved by the speaker and co-workers in 1941. The solution of the protein to be studied passes through a column of suitable adsorbent. The presence of various components in the solution produces unequal concentrations, which can be observed in the filtrate as distinct zones by the use of optical methods. The diagrams thus obtained permit observation of the separation of amino acids, peptides and fatty acids, facilitating the determination of their nature and of their concentration. These studies by the speaker and his school have widened the knowledge on the mechanism of chromatography and have allowed the analysis of complex mixtures of peptides, like those which may be obtained by enzymatic digestion of various proteins.

Medicosurgical Society

The Medicosurgical Society of Pisa convened under the chairmanship of Prof. C. Cassano. Drs. Tronchetti and Torsoli reported on their study of the influence of pituitary adrenocorticotropic hormone (ACTH) on respiration and sugar metabolism in the normal person and in hyperthyroid patients. The following observations have been made after administration of the hormone: (1) a tendency to hyperglycemia on fasting, with increase of urea in the urine, (2) a low glycemic curve after oral administration of dextrose and epinephrine, (3) decreasing basal metabolic rates in hyperthyroid patients with a low respiratory rate and (4) an increase of urinary oxygenated steroids. The interpretation of these results is still dubious. Dr. Di Molfetta discussed the pathogenesis of congenital lymphangioma cysticum of the neck. From observations in two newborn infants, operated on successfully, the speaker maintains it is possible to reach a more precise understanding of the disease by taking into consideration the development of the lymphatic system. He is of the opinion that the disease starts and develops in the mesenchyma, from which the cervical lymph node develops, and that it is characterized by a modification of the formation procedure and of the evolution of this vessel-forming center.

Drs. Luciani and Merlini discussed their experience in the treatment of brucellosis melitensis with stock vaccine and autovaccine, streptomycin combined with sulfadiazine, aureomycin and chloramphenicol. They stressed in particular their results with chloramphenicol therapy. With a dose of 3 Gm. per day, they obtained defervescence in an average of five days, without toxic phenomena of importance or signs of drug intolerance. The tolerance of chloramphenicol proved to be better than that of aureomycin, while the therapeutic results were almost the same. The speakers systematically combined chloramphenicol treatment with vaccination, stressing that this can be done with safety after defervescence had been obtained with chloramphenicol. This combination of chloramphenicol and vaccine proved to be the method of choice.

Drs. Conti and Andreani reported the results of their study on lipemic variations produced by prolonged treatment with pituitary adrenocorticotropic hormone. They observed that intramuscular injection of large doses of pituitary adrenocorticotropic hormone is followed by hyperlipemic or hypolipemic reactions. The total lipids and cholesterol are constantly increased in the patients with hypopituitarism, while rapid diminution of lipemic values occurs in hyperpituitarism. In both instances a constant diminution of total lipids and cholesterol was observed after prolonged treatment with pituitary adrenocorticotropic hormone. The speakers rather exclude the possibility that the lipid and cholesterol variations induced by corticotropic stimuli should be attributed only to the metabolic modifications of the adrenal cortex, which had been stimulated to a more active production of the steroid hormones. They admit that such variations represent manifestations of the general lipid metabolism, induced and sustained by the reactivated function of the adrenal cortex. The speakers proposed the hypothesis that in the state of depressed prehypophysial function the adrenal cortex activates, but only transitorily, the mobilization of fat deposits, with limitation to the first phase of functional recovery. In every case lipopexia is stimulated by the adrenal cortex. The fat-regulating property of the adrenal cortex is also influenced by hepatic function. The patients with chronic liver disease did not manifest significant lipid variations after administration of pituitary adrenocortcotropic hormone.

BELGIUM

(From a Regular Correspondent)

LIÈGE, Oct. 10, 1950.

Unification of Aviation Health Measures

Belgium, France, Luxembourg, the Netherlands and the United Kingdom have agreed that, beginning Feb. 1, 1950, they will be regarded as a single territory in matters of sanitary control of air transportation. From the administrative point of view, this territory will be known among the countries of the Treaty of Brussels as the "free health zone." This new system, which is the result of efforts of the Public Health Committee of the Organization of the Treaty of Brussels, makes possible the simplification of control measures, without reducing their effectiveness. The principal points of the regulation are as follows: 1. Any airplane departing from any point of the "free health zone" will, under normal conditions, be exempted from health control measures on arrival at another point in the zone. This implies the elimination of the health declaration issued by the air command for the airplane, as well as the individual declarations on the origin and health of the passengers. 2. The health control of the crew and passengers of a plane bound for the "free health zone," coming from an airport located outside this zone, will be performed only at the first stop inside the zone. The "free health zone" can, in case of an epidemic, be restricted by the ministers of public health.

Seasonal Etiology of Retinal Detachment

Dr. Van Lint has just published in *Bruxelles-Medical* an interesting study on the influence of the seasons on detachment of the retina. He asks, "Why does the spring and summer favor detachment of the retina?" All the statistics collected so far, show that there is a seasonal factor. Three causes may contribute to it in the spring: 1. Light. 2. Movement. The active or passive movements of the whole body are frequently the cause of the detachment. The arrival of spring brings an increase of walking, running, jumping, outside activities and sports. The author cites Jeandelize, who reports detachment of the retina immediately following an energetic muscular exertion, and Vogt, who observed detachment in a myopic patient after a trip by motor car. It is also well known that movement is harmful after operation for detachment. 3. A secondary cause which deserves consideration is springtime asthenia, which appears after overwork during the winter. The author suggests, therefore, that one diminish the glaring brightness of spring with adequate glasses. Myopic persons should be advised on the health aspects of movement; they should avoid jumping, long trips, falls and, in general, any effort which causes congestion in the head.

Criminality in Belgium

At a session of the Society of Neurology and Psychiatry, Leroy, after presenting a historic survey of the economic and social development of Belgium, cites the great measures for social protection which were started under the reign of Maria Theresa (the separate system of prison discipline at Ghent). He then reported the results of the law of social protection of 1930. Criminality has diminished more than 50 per cent. Contrary to the ideas of Lombroso, the number of repeated offenses decreased simultaneously with the number of first offenses, although more slowly. This constant improvement, in spite of social depressions, is due to the rising standard of living of the masses and to the improvement in education. At present, 78 per cent of the delinquents are illiterate or poorly educated and, according to the author's experience, are mentally weak or unbalanced. Social improvement is best effected by more widespread education and better mental hygiene.

Belgian Society of Endocrinology

This society has just been organized. The number of meetings will be limited to three or four a year. The reports of the Belgian Society of Endocrinology will be published in collaboration with the French society.

NORWAY

(From a Regular Correspondent)

OSLO, Oct. 7, 1950.

Heart Disease Discovered by Mass Radiography

In the Scandinavian countries, mass radiography of whole sections of the community has hitherto usually been undertaken in a search for tuberculosis. Frequently hitherto overlooked heart disease is discovered. In Stavanger, the fourth largest town in Norway, Johan Riis has lately shown that among 36,000 persons over the age of 14 examined in this way, there were as many as 290 with signs of heart disease. On closer examination of 286 of these persons, 268 were found to have heart disease; this diagnosis could not be confirmed in the remaining 18. Among the 250 were 179 over the age of 60. There were 88 with valvular disease of the heart, usually rheumatic, and 163 with high blood pressure as well as heart lesions. About one third of all these persons (92) were already aware of their heart disease. About one fifth were in need of immediate treatment.

In Stockholm, Westman found radiologic signs of heart disease in 328 persons under the age of 60 out of a total of 63,877 persons undergoing mass radiography. Among these 328 persons were 111 with acquired valvular disease of the heart, usually rheumatic. There were 59 with high blood pressure combined with cardiac lesions and 53 with congenital heart disease. About one third were unaware of their heart disease, though most of them had experienced symptoms suggestive of it. In many cases there had indeed been pronounced symptoms, but a physician had not been consulted for fear he would confirm suspicions.

Commenting on this state of affairs, Dr. O. Jervell of Oslo draws attention to confirmatory observations elsewhere, including the United States. He quotes White as estimating that about 2 per cent of the inhabitants of Northern United States suffer from heart disease. With mass radiography revealing heart disease in about 1 per cent of all the persons examined, it would seem that about every other case of heart disease would be incidentally discovered. Dr. Jervell is not quite sure this is an important advance, for he does not have blind confidence in wholesale radiologic diagnoses; even the electrocardiographic signs of heart disease are not, in his opinion, always a true index of real heart disease. "Whatever the methods we employ for the mass examination of healthy persons, we must not attach too much importance to findings differing from the normal."

National Antituberculosis Association

This summer the Norwegian National Antituberculosis Association celebrated its fortieth anniversary in Bergen. The association's president, Dr. Harold Bjelke, took this opportunity to trace its history and review its achievements. The Norwegian Medical Association was originally responsible for the foundation of this national organization in the fight against tuberculosis, and at first its direction was almost entirely in the hands of doctors. Bit by bit laymen have come to take a more active part, and at present the policy of the association reflects the layman's as well as the doctor's point of view. Since its modest beginning in 1910, the association has learned to handle seven-figure budgets which would have staggered its founders. Apart from the millions received as a voluntary organization, there are the substantial contributions made to the association by the state. Yet the greatest source of revenue has come year by

year from the small sums collected at bazaars, lotteries and small festive meetings in out-of-the-way localities. In 1928, a postmaster in a small post office began to collect used postal stamps and to send the sums from their sale to the national association. Others followed his example, and now the collection and sale of such stamps has developed into a veritable industry.

During these past fruitful 40 years annual deaths from tuberculosis have declined from more than 6,000 to less than 2,000. Norway has now more than 100 tuberculosis homes with over 3,000 beds and 20 sanatoriums and coast hospitals with some 2,000 beds, with consequent negligible waiting lists. The association was subjected to unexpected stress during the German occupation of Norway. BCG vaccination, to which the association was already pledged, was to be side-tracked, according to the head of the Norwegian Public Health Service and the association was to pass over to other bodies the system of tuberculosis nursing which had already proved so effective in its hands. The board of management of the association, however, adopted an attitude of passive resistance, with the result that the continuity of its policy was assured when, in 1945, the Quisling government of Norway collapsed with the expulsion of the Germans.

The layman has much influence in the councils of the association. It is the educated layman who has contributed so largely to the education of the public. This educational factor made itself felt when, in 1947, legislation was introduced for compulsory vaccination with BCG. It received such support from popular health education that anticipated opposition did not materialize. In county after county, persons between the ages of 15 and 40 are undergoing BCG vaccination. In 1949, in the County of Østfold alone, 92 per cent of the population at the school-leaving age submitted voluntarily to this measure. It may be pointed out that the BCG legislation of 1947 was coupled with provision for the compulsory mass radiography of the community.

Clinical Studies of Malignant Hepatitis

At Medical Department B of the Rikshospital in Oslo there was an instructive collection of cases of malignant hepatitis during the years Norway was occupied by the Germans. Prof. H. A. Salvesen, who is in charge of this department, and Dr. Ola Lödöen have published an account of these cases (*Acta Med. Scandinav.* **137**: 305, 1950). Their material consists of 23 cases in which the hepatitis lasted more than three months or ended fatally with the picture of acute or subacute yellow atrophy of the liver. All but three of these patients were women, and all the cases in females occurred between 1941 and 1946. During the same period there were only 14 patients (7 men and 7 women) with benign hepatitis observed in the same hospital department. Evidently patients with hepatitis in Oslo are not as a rule admitted to the hospital unless the disease is of long duration or has shown alarming symptoms.

An interesting question raised by Professor Salvesen and Dr. Lödöen concerns the etiology of malignant hepatitis. Is it, as argued by Alsted, distinct from the ordinary sporadic and epidemic hepatitis seen in peacetime, or are these two conditions merely variations in degree of one and the same disease? Salvesen and Lödöen admit the impossibility of final conclusions as long as the causative agent is unknown, ". . . but we are inclined to believe in the unity of the malignant and the usual peacetime hepatitis, chiefly because all the different types of development observed in the malignant form also have been seen in benign hepatitis, although by different observers. It is the mass action of many cases with these uncommon types of course of the disease which impresses the clinician, so that he thinks he observes a new disease."

COLOMBIA

(From a Regular Correspondent)

BOGOTÁ, Aug. 18, 1950.

Antituberculosis Campaign

Dr. J. P. Leyva, head of the tuberculosis department of the Ministry of Hygiene, recently gave the following statistical data on the antituberculosis campaign in Colombia. There are 25 clinics in the country for the diagnosis and treatment of tuberculosis. In these clinics 67,312 intravenous injections, 134,579 intramuscular injections, 3,278 initial pneumothorax treatments and 38,261 insufflations were administered during 1949, in which year 385,120 persons had roentgen examinations of the chest. The results were positive in 4,923 persons, suspicious in 8,688 and negative in the rest. There are four tuberculosis sanitariums and a number of tuberculosis wards in general hospitals, where 7,851 bed patients were cared for and 1,323 surgical operations done in 1949. The mortality of these hospitalized patients was 1,335. In the national campaign 629,873 persons were handled during the year and the clinical laboratories and the vaccination centers made 16,540 examinations of sputum and 85,590 tuberculin tests. The fact that 150,000 tuberculous patients have not had medical aid is due to the magnitude of the problem rather than to deficiencies of the campaign.

Mosquitoes of Eastern Colombia

Dr. Julian de Zulueta of the Roberto Franco Institute of Tropical Diseases in Villavicencio has published (*Am. J. Trop. Med.* **30**:325 [March] 1950) a study of the habits of mosquitoes in the savannas of Eastern Colombia. The observations were made during the rainy season, in June, July and November, 1948, and June 1949. He estimated that there were about 3,000,000 mosquitoes per square kilometer. The Anopheles, about 300,000 per square kilometer, included A. peryassui, A. pessoai, A. punctimacula and A. parvus. The commonest culicine species were Culex chrysotonum, Culex (melanoconion) sp. and Psorophora confinnis. The maximum distance between the site of capture and a breeding place was 1,800 meters. The mosquito count in the vicinity of the breeding place was approximately the same as the count 1 kilometer away. Biting activity of mosquitoes started shortly after sunset, continued during the night and increased slightly before sunrise; there was practically no biting activity during the day. Swarms of culicinae were seen over the savannas as early as 5 p. m., but mating of Anopheles was observed on only two occasions, at 7 p. m.; swarming males captured proved to be A. peryassui.

Personals

A new board of directors of the National Academy of Medicine of Colombia has been appointed for the period 1950-1952: Dr. Jose Vicente Huertas, president; Prof. Edmundo Rico, vice president; Dr. Augusto Gast Galvis, secretary, and Prof. Guillermo Uribe Cualla, treasurer.

Dr. Alfredo Luque B., professor of therapeutics and medicine, recently was appointed dean of the school of medicine of the National University of Colombia.

Dr. Alonso Carvajal Peralta, professor of the urological clinic of the school of medicine of the National University of Colombia, was recently appointed minister of hygiene.

The "Cruz Camilo Torres" was awarded by the national government to Drs. Emilo Robledo Correa and Miguel María Calle, both of Antioquia, on their completion of 50 years of professional work. These men are the first to receive this award, which was established Oct. 5, 1948.

Dr. Ernest Carrol Faust, professor of tropical diseases and hygiene, Tulane University of Louisiana, New Orleans, U. S. A., visited the school of medicine of the National University July 4-6. He delivered lectures to the school of medicine and to the Academy of Medicine of Colombia, on malaria in America and on amebiasis.

CORRESPONDENCE

CANCER OF THE BREAST AND ESTROGENIC THERAPY

To the Editor:—In the article "Cancer of the Breast: Classification of Cases, Criteria of Incurability and Treatment," by U. V. Portmann (*J. A. M. A.* 144:513 [Oct. 14] 1950), there are two statements which may need amendment or correction.

On page 516, first column, the next to last paragraph starts: "Although it has been proved that administration of estrogens may induce cancer of the breast and stimulate growth. . . ." Any thorough review of the subject will reveal the fact that cancer of the breast has been induced by estrogens only in especially sensitive strains of rats that were inbred in order to have a highly hereditary tendency to breast cancer. These results were obtained only with massive doses of estrogens which are in no way comparable to the doses used in human application. Nobody disagrees with the theory that estrogens probably stimulate growth of preexisting breast cancer, but the unqualified statement quoted from Dr. Portmann's paper may lead to considerable confusion and should, I believe, be properly amended.

In the last two lines of the same column the author says, "My associates and I give testosterone propionate in doses of 50 to 100 mg. intravenously three times a week." As testosterone propionate is not soluble in water, but only in oil and similar solvents, and rather poorly at that, I am afraid that 1 or 2 cc. of oil administered intravenously, just once, will not allow much further continuation of therapy. Undoubtedly the author meant to say "intramuscularly" and the error was missed in the proofreading. (A correction was published in THE JOURNAL Oct. 21, page 701.—ED.)

CARLOS P. LAMAR, M.D.,
1010 Huntington Building, Miami 32, Fla.

IRRITANT ACTION OF IODOACETIC ACID

To the Editor:—Two cases of bullous dermatitis due to contact with iodoacetic acid were reported in THE JOURNAL of March 18 (page 805). It has been suggested that the chemical acted as a primary irritant, although the possibility of a sensitization mechanism has not been ruled out in these two cases. In the past we had opportunity to carry out experiments which established the fact that iodoacetic acid acts as a primary irritant. A biochemist noted the appearance of small blisters on his hands and traced them to contact with minute crystals of iodoacetate, commonly used as an enzyme inhibitor in biochemical studies. Control experiments with iodoacetate patch tests in nonexposed subjects revealed that even a 10 minute contact was sufficient to cause a painful bullous lesion at the site of application, followed by superficial epidermal necrosis and scarring in all subjects tested.

From the studies of Peters and co-workers on the biochemistry of skin in "Modern Trends in Dermatology" (edited by R. M. B. McKenna, London, Harper & Brothers, 1948) and of Dixon and Needham (*Nature* 158:432, 1946) the mode of action of iodoacetate may be explained as follows: A large variety of sulfhydryl inhibitors, such as lewisite, mustard, methyl bromide and nitrogen mustard, cause blister formation most probably through inactivation of the free sulfhydryl groups of certain essential glycolytic enzymes (hexokinase, pyruvate oxidase). It may be assumed that iodoacetate, one of the most potent sulfhydryl inhibitors, acts by a similar mechanism. This view is supported by the histochemical observation that the sulfhydryl groups of the epidermis are inactivated by iodoacetamide (Goffart, M.: Interaction of Vesicants, Oxidizing Agents and Metal Ions with the Sulfhydryl Groups in the Skin (*Arch. internat. de pharmacodyn. et de thérap.* 74:9, 1947).

PETER FLESCH, M.D., and SHELDON B. GOLDSTONE, M.D.,
Hospital of the University of Pennsylvania, Philadelphia.

REQUESTS FOR REPRINTS

To the Editor:—Physicians, those interested in investigative work in particular, have devised a penny postcard system by which they save themselves time and money in securing reprints of articles. It would be no more difficult for these efficient penny postcards to be written so that the name and address of the person requesting the reprint appear on the lower portion of the card so that this section of the card could be detached and pasted on the envelope in which the reprint is sent. This would not only save time for the author who does not have a secretary but would facilitate the delivery of the reprint because the correct name and address would be on the envelope. The author should use a good grade of glue when affixing the detached section of the card onto the envelope.

SAMPLE CARD

Date

Please send me reprints of your article entitled

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which appeared in.....

Yours truly,
DR. H. BLANK

detach along this line

DR. H. BLANK
352 BLANK AVE.
MINEA, ILL., U.S.A.

HANS G. KEITEL, M.D.,
Massachusetts General Hospital,
Fruit Street, Boston 14.

INSPECTION OF HOSPITALS

To the Editor:—I have been instructed to send you a copy of a resolution passed by the Kalamazoo Academy of Medicine at their last regular meeting, Oct. 17, 1950. The resolution is as follows: "The Kalamazoo Academy of Medicine heartily endorses the editorial in THE JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION of Sept. 30, 1950, on "Inspection of Hospitals by Hospitals" and that a copy of this resolution be sent to the superintendent of Bronson Methodist Hospital, Kalamazoo, Mich.; the Board of Trustees, Bronson Methodist Hospital, Kalamazoo; Superintendent of Borgess Hospital, Kalamazoo; Michigan Hospital Association; the Secretary of the Michigan State Medical Society, and the Editor of THE JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION.

G. H. RIGTERINK, M.D.,
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Kalamazoo, Mich.

Council on Medical Education and Hospitals

The following statement was adopted on Nov. 1, 1950 by the Joint Committee on Medical Education in Time of National Emergency representing the Council on Medical Education and Hospitals of the American Medical Association and the Association of American Medical Colleges. This statement has been submitted to the National Advisory Committee on the Selection of Doctors, Dentists and Allied Specialists to the Selective Service System and the Health Resources Advisory Committee to the National Security Resources Board.

DONALD G. ANDERSON, M.D., *Secretary.*

MEDICAL EDUCATION IN TIME OF NATIONAL EMERGENCY

The mounting tension of the times confronts medical education with great responsibilities. Only physicians trained as highly as the state of medical knowledge and available resources will permit can serve the national interest well, whether this be in a military or in a civilian capacity. In full recognition of the need of both the armed forces and the civilian population for good medical care, as many well trained physicians as possible should be produced. To accomplish this aim in time of emergency, the following proposals are offered by *The Joint Committee on Medical Education in Time of National Emergency,* which represents the Executive Council of the Association of American Medical Colleges and the Council on Medical Education and Hospitals of the American Medical Association. These proposals have been formulated in order to profit from the experiences of World War II, to avoid a repetition of the mistakes made then and to attempt to prevent the occurrence of new errors.

The duration of the emergency on which we have entered, and of the policy of limited mobilization are at this time quite unknown. The longer or more serious the emergency, the greater will be the demand for physicians—for well trained physicians. One of the hard lessons learned from the medical training program employed in World War II was that in the national interest demands for speed and quantity should never be permitted to interfere with quality.

It is, consequently, especially important that no steps be taken at the beginning of the present emergency that will interfere with the adequate training of physicians, either as medical students or as interns and residents, or with the supply of properly trained basic scientists. If, as now appears probable, the emergency bids fair to be prolonged over many years, we must exercise great care that, in instituting measures necessary to meet the pressing and immediate demands of the emergency, we do not interfere with the continuous training of physicians. Such training requires an uninterrupted supply of students through college into and through medical school and hospitals; it requires a smaller but vitally important supply of graduate students in the basic and clinical sciences; and, it requires, also, the maintenance of an adequate basic science, as well as clinical faculty. It requires continuation of the principles of individual student participation and instruction which are basic to good medical education and which would be vitiated by acceleration, overcrowding of students or loss of faculty to the point where attention to the individual student would be diminished.

At a time when the armed forces and the civilian population both at home and abroad are demanding doctors, it is the responsibility of the medical schools to outline the conditions necessary in a critical period to the adequate training of doctors so that they will best be able to serve society. These proposals attempt to outline these conditions as they apply in a time of national emergency.

Depending on the degree of emergency, three possible methods of organization of our society might be instituted:

1. Partial Mobilization
   a. Limited mobilization (as in effect now)
   b. Extensive mobilization (as in World War II)
2. Total Mobilization (as under a National Service Act)

The primary emphasis in the proposals which follow is on policies and procedures in periods of *Partial*—and not of *Total*—mobilization. Should total mobilization be adopted as a national policy, students, faculty and physicians would then be assigned to civilian or military duty or to study, teaching or research. This would probably remove the stigma from those not in military service and not wearing a uniform. It is, however, our earnest hope that adequate mobilization of national resources and manpower can be achieved without the necessity of recourse to total controls. The proposals herewith submitted are, however, adaptable to a program of total mobilization, should this be imposed.

Whether or not the country is engaged in waging war, it is probable that a state of national emergency will be long lasting. Since well trained physicians will continue to be required, the provisions necessary to guarantee the quality of their training will apply to the problems of recovery and reconstruction following cessation of military activities, quite as much as they do in a time of immediate emergency. Problems relating to transition from a time of emergency to a state of peace will be studied by the Joint Committee when some picture of the conditions likely to be prevailing at that time becomes visible. The medical profession and the medical schools stand ready to make all adjustments needed to meet the emergency. Medical schools, hospitals and other civilian institutions should study carefully the problem of utilizing personnel with maximum efficiency in the discharge of their responsibilities to the nation and should be prepared, whenever necessary to redefine in the light of these studies, their needs for medical manpower. The governmental services should likewise continually reexamine their utilization of medical manpower to the end that an expanded military establishment will not impair the health of the nation by unnecessarily disrupting the training of physicians or widely or irregularly withdrawing doctors from the care of the civilian population.

Since physicians trained by the medical schools, universities and hospitals are as essential to the government as are the graduates from the military service schools, it is encumbent upon the Federal government to guard the integrity of medical education in time of emergency, as in time of peace. The need for hasty mobilization occasioned by the Korean war has led to irregularly extensive withdrawals of professional personnel, a process which should be controlled now by the immediate utilization of central and local committees empowered to adjudicate national and local questions of availability and essentiality of medical manpower.

Proposals

1. *Deferment of Preprofessional College Students.*—A procedure for deferment of preprofessional college students in the field of medicine, dentistry, veterinary medicine and osteopathy is provided by Selective Service Local Board Memorandum No. 7. A broader plan for deferment of college students in all fields of study has been recommended to General Hershey by the five Scientific Advisory Committees to the Selective Service System and by the Healing Arts Educational Advisory Committee of the Selective Service System and has been approved by him in principle but is still under study and has not been adopted as official policy. This plan is based upon (*a*) the standing of students in the freshman and subsequent years of college and (*b*) a scholastic aptitude test. This test should be administered by a nationally recognized testing service, such as the Educational Testing Service of Princeton, N. J. This broader plan is enthusiastically endorsed by the Joint Committee. The Committee urges prompt adoption and implementation of this plan. The Joint Committee is not favorable to the policy of identification and selection by medical schools of college students as "premedical students" early in their college careers, which appears to be implied in the following sentence in the new law for induction of medical, dental and allied specialists:

"It is the sense of the Congress that the President shall provide for the annual deferment from training and service under this title of numbers of optometry students and premedical, preosteopathic, preveterinary, preoptometry and predental students at least equal to the numbers of male optometry, premedical, preosteopathic, preveterinary, preoptometry and

predental students in attendance at colleges and universities in the United States at the present levels, as determined by the Director."

The Joint Committee recommends that students desiring to study medicine be included in the broad deferment plan for college students mentioned above.

2. *Duration of College Training.*—So long as the national circumstances permit the basic structure of collegiate education to continue undisturbed, four years of college training prior to entrance into medical school is desirable. In an emergency requiring extensive mobilization, the period of college training prior to entrance into medical school could be reduced to ninety semester hours, contained in three academic years of college training. This would involve 90-110 weeks of actual study.

The curriculum for those planning to enter medicine should be kept flexible during the college period. The emphasis should be on developing the students' capacities and attitudes quite as well as on instilling specific scientific knowledge. The student must continue to demonstrate superior performance in the courses that are regularly required for admission to medical school.

3. *Selection of Medical Students.*—The selection of all medical students, and, we believe, of all professional students, should be in the hands of the individual professional schools, for only in this way is it possible to secure the best candidates for medical study. The period for accepting applications and commencing and concluding the acceptance of medical students should be as uniform as possible.

Qualified individuals on active duty who secure permission from the Armed Forces, Public Health Service or Veterans Administration to apply for admission to medical school should be eligible for consideration with other candidates for admission. If accepted for admission, we believe that such students should be placed on inactive duty during the period of medical training, including undergraduate and graduate phases. During this training, they could wear special identifying insignia.

A satisfactory mechanism for the deferment of medical students who are registrants with the Selective Service System is provided at present by Local Board Memorandum No. 7.

On the basis of experience with the AST and V-12 programs in World War II, we believe very strongly that it is neither desirable to place medical students in uniform nor to have them subsidized as a group by the government. It might be wise to have a special insignia which could be worn by the students to indicate that they have been deferred, or, if commissioned, placed on an inactive duty status, for study considered essential to the health and welfare of the nation.

In place of such induction and full payment of medical students as was conducted under the AST and V-12 programs in World War II, we believe consideration should be given to the inauguration of a system of governmental scholarships which would be available to students on the basis of economic need or as a reward for academic superiority. A program providing government loans should also be considered. The medical schools should be charged with the responsibility of selecting the recipients of these scholarships or loans.

Medical schools should, of course, continue to accept properly qualified female students and properly qualified male students who may be physically unacceptable to the armed services.

4. *Obligation of Medical Students to Serve Their Country Following Graduation.*—The status of students and their obligation to serve will, it is recognized, depend on national circumstances. A plan should be devised which will define clearly the obligation of students who have been deferred for professional study to serve the government subsequent to completion of their training. *Deferment* should not indicate exemption from government service, but merely *delay or postponement* of service. Students deferred by the Selective Service System should on completion of hospital or other graduate training and on certification of availability by such appropriate agencies as the National Advisory Committee on the Selection of Doctors, Dentists, and Allied Specialists to the Selective Service System and the Health Resources Advisory Committee to the National Security Resources Board be obligated over a period of years to serve when needed in such federal services as the Armed Forces, Public Health Service or Veterans Administration hospital program for a period consistent with the obligation of others for military service. The certification of availability referred to above should be made after consideration of the civilian, public health and welfare needs, including essential research and teaching. Deferment, therefore, has as its only objective a later service in a needed capacity.

As this problem is being studied by appropriate government agencies, representatives of the medical schools and the medical profession should participate in the formulation of policies.

5. *The Medical School Curriculum.*—The continuous 36 month accelerated program in the medical schools during World War II was almost universally recognized as a major cause of production of poorly trained doctors. It was exhausting to students and faculty alike and developed immature physicians. Such a program of acceleration could not be reinstated in the present emergency without very serious disruption of the training of physicians, not only for the reasons stated above, but also because at least one-third of the medical schools have now extended one or more of their academic years from 9 months to 10, 11 or 12 months. This is because the extension of knowledge has made it appropriate for some schools to increase the length of their basic science years and because many schools have found it necessary to utilize an 11 or 12 month third or fourth year, or both, in order to provide adequate training in public health, psychiatry and other newly emphasized disciplines. Indeed only by using their clinical facilities over this extended period have a number of schools found it possible to provide an adequate training in medicine and surgery and other clinical subjects.

For the majority of medical schools the committee recommends as an essential during an extensive emergency or war that the curriculum extend over four 12 month years. This would permit continuation of the program already under way in many schools. It would also provide opportunity for inclusion during extended academic years or special periods of new material essential for national welfare and security, especially in time of emergency. Studies of atomic energy, radiation sickness and protection, blast injury, bacteriological and chemical warfare, the handling of mass casualities and other aspects of civilian defense, special problems in epidemiology, industrial medicine and hygiene, rehabilitation and utilization of manpower, military medicine, tropical medicine and needed military procedures would be included. Consideration by the Joint Committee of the content of such studies is under way in consultation with representatives of the Surgeon General of the Public Health Service, the Director of Medical Services, office of the Secretary of Defense, the Surgeons General of each of the Armed Forces, the Chief Medical Director of the Veterans Administration, the Director of the Health Resources office of the National Security Resources Board, the Medical Schools and the Medical Film Institute. It is already clear that some of the material can be integrated into the existing curriculum; it is equally clear that new time, new courses, new teachers must be found if medical students are to be trained adequately in these important areas.

During a period of extensive mobilization, it is probable that students will not be deferred during long summer vacations. If the college year ends in June, medical schools operating under the proposed four 12 month year curriculum might, therefore, be expected to begin in July. Students would then graduate from medical school in June at the end of four 12 month years. As long, however, as vacation is permitted after completion of college, and medical schools continue to commence in September, three 12 month and one 9 month year are recommended. The few schools which elect to operate on an accelerated program should, of course, be free to continue to do so. In any of these programs, summer vacation periods, normally three months in length, could be limited to one month at the end of the freshman year and either one month or two weeks at the end of the second and third years, the remaining two weeks being inserted at the end of quarters or semesters during the school year.

Many schools would doubtless wish to incorporate much of the new material into their regular courses or clerkships, extended in length. Others might wish to devote two month periods either in the summer or between quarters or semesters to special study given either by their own faculty or perhaps by representatives of governmental agencies. During such periods in schools where R.O.T.C. programs are in effect, students could be sent to a camp or a clerkship in a military hospital. In such periods some groups might be sent to special centers or schools for instruction in atomic medicine or civilian defense. Some schools operating on an accelerated program might wish to place such special instruction at the end of the established academic program. The final program should be that which in the judgment of each school is most consistent with its program of maintenance of high standards of medical education and the promotion of the public welfare. At the end of such a four year program, graduating physicians would be more mature, better trained in their profession and also have basic training in matters of public health, civilian defense and military medicine. When, in addition, they complete their hospital and graduate training, they should be prepared for duty necessary to the national health, safety and welfare without the necessity of preliminary orientation, even after entrance into active military duty.

6. *Number of Students in Medical School.*—Since the end of World War II the medical schools, by expanding their facilities and faculties, have been able to increase the number of students admitted annually from a prewar average of 6000 to over 7000. It is recognized that in an emergency of any duration a further increase in production of physicians will be necessary. Since most medical schools are today maximally expanded and some even over-expanded, it is clear that, in order to produce more physicians, they will need more faculties and facilities. To accomplish this would require additional funds and additional teachers. It is clearly the obligation of each school to explore anew its resources with a view to determining, if possible, how and to what extent it can increase its output without lowering quality and what it will require to do so.

It should be obvious that the depletion of existing faculty through service in the Armed Forces of significant numbers of active teachers, including graduate students and hospital residents, such as occurred in World War II, would not only reduce the quality of present teaching but would work in direct opposition to any program for increasing the supply of physicians. Such depletion might, indeed, necessitate a reduction in enrolment in medical schools.

7. *Faculty Requirements.*—The maintenance of adequate faculties is essential if medical schools in a national emergency are to meet the demands placed on them for the education of medical students, the advanced training of physicians, basic scientists, investigators, and new teachers; for the prosecution of research important to the national health, safety and welfare; and for the training of ancillary personnel in the health services.

To maintain the faculties of medical schools at proper strength for the accomplishment of these objectives, it is imperative that there be established without delay an effective, coordinated and enlightened program regulating the entrance into military duty, both on a voluntary and on an involuntary basis, of those who constitute the faculties of the medical schools. This program should be so designed that the stigma of evasion will not be attached to those deferred for essential activities related to medical education. It is urged that the National Advisory Committee on the Selection of Doctors, Dentists and Allied Specialists to the Selective Service System and the Health Resources Advisory Committee to the National Security Resources Board formulate without delay, for the guidance of local advisory committees, principles and policies governing this important phase of the selection and distribution of physicians between the civilian population and the armed services.

The actual selection of individuals at all levels, in conformity with these principles and policies, should reside in local communities, organizations and institutions, so far as education is concerned in medical schools and teaching hospitals. It is strongly urged that the local committees in areas in which medical schools are located include the deans of such schools or their representatives. The educational institutions, with which this statement is particularly concerned, should be directed to assess and report not only their minimum needs for continuing operation, but also their capacity to expand and the requirements for such expansion without deterioration of quality of education.

The minimum faculty essential for the conduct of a satisfactory program of medical education must be carefully safeguarded and maintained. This minimum will vary from medical school to medical school and will depend on many factors such as the size of the school and its other responsibilities for research, for medical service and for the teaching of groups other than undergraduate medical students, e. g. graduate students, practicing physicians and students in other colleges of the university of which the medical school is a part.

This minimum number of essential teachers obviously must be related to the size of the normal peacetime faculty of the medical school; e. g., some medical schools can release very few faculty members without seriously handicapping their teaching program, while other medical schools, particularly those with relatively larger faculties, can release more without deterioration in the quality of their instructional programs. On the other hand certain schools ought to add faculty members.

Local and state advisory committees to the Selective Service System should be required to discover the needs of the individual medical schools for faculty members both for undergraduate medical student instruction and for the other essential activities carried out by the medical schools and to make adequate allowance for these needs.

In time of limited or extensive mobilization the problem of faculty morale is a difficult one. Essential teachers who are liable for military service must either be deferred or inducted and assigned on inactive duty to the medical school. There are, however, those among the faculty who are unwilling to be declared essential. Some of these might be appointed consultants to military hospitals in the vicinity so that they may be of service from time to time on a temporary duty status. Some may be allowed to enter service. For these, however, the period of active duty should be for a clearly limited period of time, such as two years, after which they should be returned to the faculty. In their military assignment consideration should be given to their technical knowledge and skills and their ability to teach. In their place on the faculty, substitutes or exchanges might be released from active service. Such exchanges should be equivalent both as to function and competence. Such a rotation of faculty members while, of course, easier to implement in the clinical than in the basic science fields, and while presenting some problems in the development of sustained and continuing programs of instruction, would be preferable to the loss of key faculty members for tours of duty lasting four, five or more years. Perhaps a similar scheme of rotation between civilian and military duty could be extended to many practicing physicians.

Such arrangements for rotation would seem to offer great advantages in terms of (1) supply, (2) morale, (3) professional ability of medical officers and faculty alike. If faculty members on active duty had the opportunity to return to the medical schools for teaching, study and research, their incentive and skill would be increased. Likewise, their presence in the schools would be of great value in the training of students in the meaning and the value of military training.

The maintenance of a continuous supply of new faculty members is as great a need as is the continuous supply of premedical and medical students. This is true both for basic science and clinical faculty.

8. *Graduate Students in the Basic Medical Sciences.*—To maintain the flow of basic science faculty, graduate students in the basic sciences, both in college and medical school must be deferred for study, teaching and research. The failure to do this in World War II produced a severe shortage in supply of basic

science preclinical faculty, a shortage from which we will suffer and which would be seriously exaggerated if a more intelligent policy were not put into effect in the present emergency.

It is imperative that this need be kept in mind by the National Advisory Committee on the Selection of Doctors, Dentists and Allied Specialists to the Selective Service System and the Health Resources Advisory Committee to the National Security Resources Board, and by local advisory committees. It may be easier for local committees to understand the community needs for medical practitioners and even for hospital residents than for graduate and postgraduate students and basic science faculty. It is, therefore, essential that clear instructions be issued so that the significant part that men in these areas play in the production of qualified physicians is fairly evaluated and clearly understood.

9. *Interns.*—All internships should be at least 12 months in length. When feasible in light of the needs, some longer internships should be permitted. The nine month internships during World War II were universally recognized as unsatisfactory. All medical school graduates should be permitted an internship or equivalent training as graduate or postgraduate students. Interns and graduate students should be selected by the hospitals and medical schools as in peacetime.

10. *Residents.*—Residency training is a form of postgraduate education without which it is impossible to produce a continuing flow of competent teachers, clinical investigators and specialists. These residents are essential to adequate patient care in the better hospitals. Furthermore these residents constitute one of the largest and most helpful group of teachers and research workers.

It is recognized that a national emergency with its immediate demands for men will result in some limitation of residency training. It cannot be too strongly emphasized, however, that no matter how serious the emergency may become, there will always be urgent need for a program that provides for the continuous training of residents.

During World War II a percentage of residents were deferred for 9-18 months of residency. Because, however, residents completing even a full "9-9-9" experience were insufficiently trained to justify the temporary loss in medical manpower entailed in their residency training, the nine months' residency in World War II was unsatisfactory. The saving in time under the "9-9-9" program proved to be false economy.

It is now recognized that internship and residency training are as integral parts of the training of a physician as is his undergraduate medical course. Consequently a policy of indiscriminant issuance of commissions to residents who volunteer for service (under Public Law 779), without possibility of deferment to meet essential situations, would be shortsighted. Its general application might mean that, for all practical purposes, next year there would be no residents. Even if a policy of return of officers from active duty to undertake residency training is undertaken, it may be two or three years before such officers are returned. There will be a serious break in the chain of residency training. This will interrupt the training of specialists important alike to the Armed Forces and to the civilian population and will disrupt the clinical clerkship teaching of medical students.

It is recognized that opportunities for residency training should be available to properly qualified individuals who have been in active service; and that following one or two years of hospital training after graduation from medical school, many young physicians could be expected to serve on active military duty for a suitable period before returning to undertake or to complete residency training. This program should not, however, be permitted to interfere with a policy of deferment of selected junior as well as senior residents for proper training in teaching hospitals. This policy should become the immediate responsibility of the National Advisory Committee on the Selection of Doctors, Dentists and Allied Specialists to the Selective Service System and the Health Resources Advisory Committee to the National Security Resources Board who should so advise each local advisory committee so that the presently threatened disruption of the residency training program can be brought under control.

11. *Medical Education Under Universal Military Training or a National Service Act Involving Total Mobilization.*—No extensive discussion is attempted here of the effect of a Universal Military Training Program or of a National Service Act upon medical education. It is felt such a discussion should be deferred until more specific information is available concerning such programs or the possibility of their development. It must be clear, however, that even under U.M.T. or a National Service Act adequate provision must be made for a continuing flow of premedical and other science students, medical students, interns, residents and graduate students in the basic sciences and for retention of adequate faculty to supply the necessary training. The proposals which have been submitted in this report are, it is believed, readily adaptable to conditions of full mobilization under a National Service Act.

In any universal military training program which might be adopted, provision should be made for a delay in the period of required service of qualified preprofessional college students until they have completed their college and professional training or have discontinued the program. This plan should employ the principles recommended earlier in this document for the deferment of outstanding college students under the present Selective Service Act. Such students would thus be able to serve society and their government later in their special needed capacity. They should not be called upon to perform double duty for the Armed Forces.

Summary

1. To insure the continued production of well qualified medical graduates, provision must be made for an adequate supply of premedical students.

2. The duration of premedical study should not be reduced below 90 semester hours, the equivalent of 3 academic years.

3. All medical students should be selected by the medical schools.

4. Subsequent to graduation and internship, deferred medical students should, if certified as available by such appropriate agencies as the National Advisory Committee on the Selection of Doctors, Dentists and Allied Specialists to the Selective Service System and the Health Resources Advisory Committee to the National Security Resources Board, be obligated to serve when needed in the Armed Forces or other specified government services.

5. The curriculum of medical study should be reorganized to give proper emphasis to subjects of particular importance for the national health, security and welfare in time of national emergency.

6. Medical schools should exert every effort to admit as many medical students as they can train without deterioration of the quality of medical training they can provide. Provision should be made for the increased financial support essential to the provision and maintenance of the increase in faculty, facilities and buildings required to accomplish the proposed increase in enrolments.

7. The maintenance and replenishment of adequate faculties in the medical schools are absolutely essential to the continuing production of well trained physicians to meet the needs of the civilian population and Armed Forces.

8. All medical school graduates should have an internship or graduate or postgraduate training of 12 or more months' duration.

9. The continuation of an active residency training program is essential to adequate professional training, teaching and medical care, even in the gravest emergency.

10. Provision for training of young men in the basic medical sciences, including graduate training, is also essential for the teaching and research functions of the medical schools and for the prosecution of research programs elsewhere. Properly qualified personnel, whether they do or do not hold a degree in medicine, should be deferred or assigned to these activities rather than to active military duty.

Conclusion

In time of emergency, just as in time of peace, an important phase of national security—the maintenance of health—demands highly trained physicians in sufficient numbers. The objective of the present proposals is the maintenance of this supply of physicians. These proposals reflect the critical and intensive thinking of medical educators who since World War II have been studying this problem so as to benefit from the experience and mistakes of World War II. They have been developed after full opportunity to obtain the suggestions of representatives of the governmental agencies concerned. These experiences, and consequently these proposals, emphasize the fundamental truth that in medicine there can be no substitute for adequate training. It is urged, therefore, that in the best interest of the nation this principle be recognized fully in all plans for medical education that may be adopted in the present or future emergencies.

JOINT COMMITTEE ON MEDICAL EDUCATION IN TIME OF NATIONAL EMERGENCY

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Medical Motion Pictures

Subcutaneous Blood Flow in the Bat. Reel I, Vascular Patterns. Reel II, Behavior of Blood and Vascular Components. Reel III, Active Vasomotion. 16 mm., black and white, sound, showing time 30 minutes. Prepared by Richard L. Webb, Ph.D., Department of Anatomy, and Paul A. Nicoll, Ph.D., Department of Physiology, Indiana University, Bloomington. Supported in part through a research contract with the Air Material Command, Wright Field, Dayton, Ohio. Produced in 1948 by and procurable on rental or purchase from Audio-Visual Center, Indiana University, Bloomington, Ind.

These films were designed to show peripheral circulation and the nature and behavior of minute blood vessels in their normal environment. By spontaneous and induced vasoconstriction, this motion picture portrays the slow motion in blood vessels of a mammalian species. The red blood cells appear as biconcave disks, which is a distinct improvement over previous vascular pictures of the mesentery of the frog, where oval nucleated cells are seen. Vasomotion in arterioles by contraction of vitally dyed spiral smooth muscles, rhythmic contractions of the vein, functions of the valves in the veins, action of precapillary sphincters and differentiation of endothelial cells, leukocytes and thrombocytes are all well visualized. The thrombocyte and leukocyte reaction to injury is also adequately portrayed.

While these films show superb photomicrographic technic, the ideal motion picture on this subject should have interspersed short sections of animated drawings to allow the student to visualize the events taking place. The only photographic fault appears as the camera moves, when one notes a matrix of cellular debris which is apparently adherent to the lens system.

This production should be excellent for showing to physiology and biologic science students.

Each of the three reels deals with a definite phase of circulation in its respective title and may be used separately and repeatedly for intensive studies of its special province. It is suggested that the first and second reels be used as a unit and the third reel as supplementary material.

Obstetric Roentgenography. 16 mm., black and white, sound, showing time 16 minutes. Prepared in 1950 by Paul C. Swenson, M.D. and T. L. Montgomery, M.D., Departments of Radiology, Obstetrics and Gynecology, Jefferson Medical College of Philadelphia. Procurable on loan from Film Library, Jefferson Medical College, 1025 Walnut Street, Philadelphia 7.

This motion picture describes the use of a modified Colcher-Sussman technic of pelvimetry and cephalometry with emphasis on the need for pelvic classification and careful clinical correlation in interpreting the observations. Emphasis is placed on the need for observation of the fetal-pelvic relationships at the time of labor.

The flat pelvis demonstration fails to mention the external characteristics, but this is not objectionable, inasmuch as the present trend is toward evaluating internal measurements, those which are necessary for the fetal head to pass through the pelvis. Some may question the cephalopelvic disproportion sequence in one section of the film which does not appear to exist. It seems to be an increased pelvic inclination instead of a disproportion. This sequence should be clarified. There may be exception to the statement "We are now going to do a sterile vaginal examination." This terminology should be discouraged.

With these exceptions the information given in the film is accurate. It should be suitable for general medical society meetings, general practitioners, medical students and nursing education. The photography ranges from poor to good. A black background in the early scenes showing several types of pelves would have been more suitable.

Your Friend in Blue. 16 mm., color, sound, showing time 30 minutes. Produced in 1950 by Division of Public Health Education, Minnesota Department of Health. Procurable on loan within the state of Minnesota and on purchase from Visual Education Dept., Minnesota Dept. of Health, University of Minnesota, Minneapolis.

This motion picture was produced to recruit more young women for training in the field of nursing and to interest local community groups in public health nursing service. It gives an over-all view of the education, functions and services of a public health nurse in a public health program. It also offers a picture of all the services provided by a public health nurse with more detail of the nursing care of the chronically ill. Services in the rural area and small town are shown in the nurse's opportunity to serve the general community. The film illustrates cooperation among several community agencies and shows the practicing physician in the promotion of a generalized public health nursing program. Though it does not imply that a nurse is associated with the health department, the latter is available for such assistance as she might need.

The film is well suited for showing to community groups for promotion of public health nursing services where such services do not exist; for use in high schools and colleges as a means of recruitment; to orient student nurses with a generalized community nursing program, and for medical student information. It could also be used to advantage in interpretation of the public health nurse's function to private physicians and personnel of community health agencies. The defects are largely omissions; however, a single film cannot include the whole story.

An explanation of the organization of the community that sponsors such programs would have been helpful. It must be remembered that this film was produced to develop interest in and to interpret the services of the public health nursing field. It was not intended for use as an instructional tool in the technics of nursing; however, the instructors in the school of nursing could supplement the film with demonstrations of nursing technics. In some places the color is very poor and underexposed. In general, the photography is fair to excellent. The narration is satisfactory and the sound good. At times the story moves rather slowly.

Bureau of Legal Medicine and Legislation

MEDICOLEGAL ABSTRACTS

Malpractice: Standards Applicable to Drugless Healers.—The plaintiff, administratrix of her husband's estate, filed suit for damages for his death, which was alleged to have been due to the malpractice of the defendant, a drugless healer. From an adverse judgment, the defendant appealed to the Supreme Court of Washington.

For several days the deceased had been bothered by nausea and a pain in his stomach. The muscles of the abdomen were somewhat rigid. At his wife's suggestion, he went to the defendant, a drugless healer, who was of the opinion that the deceased was undergoing a "reaction." After checking with a stethoscope, the defendant applied hot and cold packs and administered an electrical massage with a device known as a "sine wave." A form of laxative known to drugless healers as a "42" was also given. The same treatment was prescribed for the next 10 days, at the end of which time the plaintiff begged the defendant to call in a medical doctor. The defendant replied, "We don't need an M.D. If you call an M.D. he will kill him." The defendant also said he would "throw up" the case if a doctor was called. The next day, after the application of more hot and cold packs and a "sine wave" treatment, the deceased regurgitated matter that the defendant said was "pieces of the bowel." Defendant then massaged the deceased's abdomen, but when he left the house he told the plaintiff that she could now "call an M.D." He said, however, that he would not stay until an M.D. arrived, because he could not "be here when an M.D. comes." A physician, called to the plaintiff's home the next morning, immediately diagnosed her husband's condition as appendicitis and had him removed to a hospital, where he was given oxygen and treatment for shock. The deceased was moribund, and his abdomen was extremely rigid and distended. An operation was performed that same day, but no attempt at exploration was made after the incision was made, for the reason that a large quantity of pus was encountered, and the doctors thought it best simply to try to drain the matter present before any further surgery was attempted. The plaintiff's husband died within a week, and an autopsy indicated that death resulted from peritonitis and that the appendix had completely rotted off from the portion of the bowel to which it is normally attached.

The Supreme Court first stated four basic propositions applicable to the case. The first of these is that the defendant is not a doctor. An examination of all the statutes bearing on the subject, said the court, nowhere reveals any reference to drugless healers as "doctors," nor will the language used sustain even a remote inference that they are permitted to practice any phase of medicine or surgery. Limitation in the statutes specifically negates such an assumption. The second proposition is that drugless healers cannot qualify as expert witnesses as to matters in the general realm of medicine and surgery. The fields of drugless healing and surgery are not coextensive, and we are here concerned with the field in medicine and surgery that lies outside of the drugless healing field. The third proposition is that drugless healers do not belong to a school of medicine. They do not study in medical colleges as defined by statute, but in drugless healing schools. Thus, the particular school of their attendance is not a medical school, nor can such a school be said to adhere to a school of medicine, in the sense that a particular school is identified with a recognized and distinct approach to medical practice or opinion. This is so, notwithstanding the fact that some subjects taught in medical schools are also taught in the drugless healing school. The legislature required drugless healers to pursue certain studies in order that they would know enough not to injure patients, and to recognize cases where their limited methods are inefficacious and the services of a doctor are required. The fourth and last proposition is that one who does not have a license to practice medicine and surgery is, nevertheless, liable for malpractice when he assumes to act as a doctor and is to be judged as if he were a doctor because of those facts. The defendant's theory that a drugless healer is licensed to treat all human maladies and must be exonerated from all liability on his part, if he resorts only to the particular methods of his cult for determining the nature of diseases and the remedies therefor, no matter how serious the consequences, cannot be entertained. If there is a reasonable general agreement as to what is the proper medical treatment for a disease or an organic disorder, the question of whether the treatment, in a particular case, was correct must be determined by the testimony of expert witnesses from the medical field, who alone are qualified to speak. While it is true that a practitioner, such as the defendant, is not, in his limited field, required to be an insurer of results any more than a doctor of medicine, still, if he steps out of his limits and undertakes to treat a disorder for which, in the highest level of medical science, there is a generally recognized treatment, such interloper must be held accountable to the accepted standard of treatment.

The defendant first objected to a hypothetical question, which the court permitted to be answered. It is as follows: ". . . if a patient presents symptoms of pain in the stomach and throughout the abdomen, nausea and rigidity of muscles in the abdomen, with temperature, and is treated for a reaction for a period of 12 days, and his condition grows much worse, should a sanipractic doctor of average skill and experience of those of the same school of practice in Spokane, Wash., and with the use of ordinary care, be led to suspect that the patient is suffering from appendicitis?" It was, said the Supreme Court, incumbent on the plaintiff to show that there had been a wrong diagnosis and that it had been followed by treatment that was injurious. It was amply clear that the deceased had many of the characteristic symptoms of appendicitis and the defendant must have been aware that appendicitis was a probability, if not a certainty. If it was appendicitis, he had no right to treat it; and, if there was a possibility that it was appendicitis, he had no right to gamble with the deceased's life, on the theory that it might be something else. The gist of the defendant's argument is that a wrong rule of law was followed with regard to the admission of evidence and the effect allowed to be given to the evidence. His position is that a doctor does not incur liability for his mistakes, if he has used methods recognized and approved by those reasonably schooled in the profession, and that the testimony of other doctors that they would have followed a different course of treatment than that followed by the defendant, or a showing of a disagreement of doctors of equal skill and learning as to what the treatment should have been does not establish negligence. We may grant, said the court, that there has been such a rule applied between doctors, but we repeat that the defendant is not a doctor. The court should not apply such a rule to drugless healers, because it is obvious that their qualifications are so far inferior to those of a doctor that the law will conclusively presume that they are not on terms of equality which would entitle their opinions to cancel out the best medical opinion available. Should any court so hold, it would bring reproach on judicial processes by departing from the time-honored rules of evidence devoted to the most trustworthy ways of revealing truth, which has always admitted the best evidence available. The rationale of the rule is applicable only where doctors who are equal in their qualifications are concerned and where no recourse can be had to higher learning or greater experts.

The defendant next contended that the Appellate Court should have given a certain instruction requested by him. Among other things, this refused instruction said, "In this connection you are further instructed that if you find from a preponderance of the evidence in this case the deceased, Morris C. Kelly, or the plaintiff herein knew at the time they appointed the defendant that he belonged to a branch of the drugless school of healing which does not follow surgery, then the plaintiff in this case cannot charge the defendant with negligence in failing to advise or perform a surgical operation as treatment for which the said Morris C. Kelly was suffering." The defendant argued

that without this paragraph the jury might have decided that it was the duty of the defendant, practicing as a drugless physician, to abandon his own method of drugless treatment in an appendicitis case and run to a surgeon for help. Such a finding by the jury would be justified as to the facts and correct as to the law, said the Supreme Court. A drugless healer is in a position of trust and confidence as regards his patient, and, if he knows or should know that any treatment he is permitted to use will be of no benefit to the patient, it is his duty to so advise. If there is another mode of treatment that is more likely to be successful, which treatment he does not have the right to give, it is his duty to send the patient to a doctor. The relationship between a physician and his patient is predicated on the proposition that the physician has special knowledge and skill in diagnosing and treating diseases and disorders. In the case at bar, the Supreme Court continued, the defendant knew or should have known that the treatment called for was beyond the scope of his license and ability. If a practitioner, such as the defendant, declines to discharge his duty to call in a qualified doctor when the situation obviously calls for it, he proceeds at his peril.

The defendant made much of the contention that the deceased had assumed the risk and was guilty of contributory negligence because he knew the defendant would neither operate nor advise an operation. The Supreme Court, however, said that, on the question of contributory negligence in such a case as the one at bar, the law is that it is not part of the duties of a patient to distrust his physician, or to set his own judgment against that of the expert whom he has employed to treat him, or to appeal to other physicians to ascertain if the physician is performing his duty properly. The very relation assumes trust and confidence on the part of the patient in the capacity and skill of the physician, and it would indeed require an unusual state of facts to render a person who is possessed of no medical skill guilty of contributory negligence just because he accepts the word of his physician and trusts the efficacy of the treatment prescribed by him. A patient has the right to rely on the professional skill of his physician, without calling others in to determine whether he really possesses such skill or not. The patient is not bound to call in another physician, unless he becomes fully aware that the physician has not been, and is not, giving proper treatment. On the basis of all the evidence, the court was of the opinion that the plaintiff was entitled to recovery and the judgment against the drugless healer was therefore affirmed.—*Kelly v. Carrol, et ux 219 P. (2d) 79 (Wash., 1950).*

Autopsies: When Court Should Permit Exhumation and Autopsy.—In an action for damages for the death of the plaintiff's husband following an automobile accident, the defendant filed a motion for permission to exhume the body of the deceased and to perform an autopsy thereon. From an order denying the motion, the defendant appealed to the Supreme Court of New Hampshire.

The defendant's motion alleged, among other things, that he was informed and believed that the deceased died of cancer and not as a result of the automobile accident in which he was involved; that permission to perform an autopsy was sought of and refused by the plaintiff; that unless an autopsy is performed the defendant will be deprived of information necessary to properly prepare and adequately defend the claims being presented on behalf of the plaintiff. The question before this court, said the Supreme Court, is whether the trial court's findings could reasonably be made on the evidence before him.

If the interests of justice demand it, the Supreme Court said, the trial court has the authority, in the exercise of a sound discretion, to order an autopsy. We agree that "the quiet of the grave, the repose of the dead, are not lightly to be disturbed. Good and substantial reasons must be shown before disinterment is sanctioned." However, the right to have a dead body remain unmolested is not an absolute one; it must yield where it conflicts with the public good or the demands of justice. In this case, continued the Supreme Court, the deceased had filed an action against the defendant for $25,000 after an automobile accident. He died 11 months after the accident, and his widow, the plaintiff, now claims his death, as well as his disability during the period between the accident and his death, was due to and caused by the accident. The defendant maintains that an autopsy is necessary in order to determine the nature of the deceased's injuries as well as the cause of his death.

It seems to us, said the Supreme Court, that an autopsy is very material to the defense of this action by the defendant; it may be vital, and the fact that the defendant might have other sources of evidence on the subject would not prevent his being granted the relief sought. We find no evidence in the record which could reasonably justify a denial of the defendant's motion for an autopsy under proper safeguards. Accordingly the action of the trial court denying the defendant the right to exhume the body of the deceased and to perform an autopsy thereon was reversed and permission therefor was granted.—*Kusky v. Laderbush,* 74 A (2d) 546 (New Hampshire 1950).

Paternity: Court's Right to Compel Submission to Blood Grouping Tests.—The plaintiff wife filed suit for divorce on the ground of desertion, and the defendant counterclaimed for divorce on the grounds of desertion and adultery, alleging that a child born to the plaintiff was not his daughter but was the result of an adulterous relationship. The defendant asked for an order requiring the plaintiff, the child and himself to submit to blood-grouping tests. The motion was heard in the superior court of New Jersey, chancery division.

The New Jersey statutes provide: "Whenever it shall be relevant in a civil action to determine the parentage or the identity of any child or other person, the court, by order, may direct that any party to the action and the person whose parentage or identity is involved submit to one or more blood-grouping tests, to be made by duly qualified physicians under such restrictions and directions as the court or judge shall deem proper." The court said that in its view the intent of the legislature in enacting the above statute reflected a recognition of "the theory that the evolution in practical affairs of life, whereby the progressive and scientific tendencies of the age are manifest in every other department of human endeavor, cannot be ignored in legal procedure, but that the law, in its effort to enforce justice by demonstrating a fact in issue, will allow evidence of those scientific processes which are the work of educated and skilful men in their various departments, and apply them to the demonstration of a fact."

In the first place, continued the court, it seems clear that the accuracy and worth of the tests has been abundantly shown. "On this point it is enough to cite the report of the American Medical Association's committee on Medicolegal Blood-Grouping Tests (*J. A. M. A.* **108:** 2138 [June 19] 1937), which shows that, although such tests cannot prove paternity and cannot always disprove it, they can disprove it conclusively in a great many cases provided they are administered by specially qualified experts." In a prior case decided by the Supreme Judicial Court of Maine the worth of these tests was recognized and it was held that where exclusion of parentage was shown by competently given tests the evidence was conclusive (*Jordan v. Mace,* 69 A [2d] 670; *J. A. M. A.* **142:** 750 [March 11] 1950). To the same effect is a recent case decided by the New York Appellate Division (*Commissioner of Welfare ex rel v. Costonie,* 97 N. Y. S. [2d] 804; *J. A. M. A.* **144:** 573 [Oct. 14] 1950). If blood tests are accurate, relevant and on their face apparently authorized by statute, continued the court, an order for such a test on proper terms should be granted.

Continuing, the court concluded that a case such as this comes within the words of the statute that "Whenever it shall be relevant in a civil action to determine the parentage or the identity of any child . . . (emphasis added)" and such a holding is not a violation of the Constitution. The health of our judicial system, depending as it does on the finding of truth so that justice may be done, is of equal importance with the physical health of the community and a blood-grouping test, made by skilled physicians, does not constitute the mythical nose of the camel under the tent which will be followed by such extreme measures as the trepanning of the skull of a witness. Accordingly the defendant's motion requiring the plaintiff, the defendant and the child to submit to blood tests by two physicians duly qualified by training and experience was granted.—*Anthony vs. Anthony,* 74 A (2d) 919 (New Jersey 1950).

CURRENT MEDICAL LITERATURE

AMERICAN

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Titles marked with an asterisk (*) are abstracted below.

American Journal of Clinical Pathology, Baltimore

20:701-800 (Aug.) 1950

Attempts to Isolate Poliomyelitis Virus from Paralyzed Muscle of Patients During Acute Stage of Disease. C. W. Jungeblut and M. A. Stevens.—p. 701.
Experimental Urolithiasis: Calcium Oxalate Stone. T. J. Domanski. —p. 707.
Mercury and Lead Storage in Human Tissues with Special Reference to Thrombocytopenic Purpura. E. M. Butt and D. G. Simonsen. —p. 716.
*Correlation of Clinical Features of Cirrhosis of Liver with Findings on Biopsy. H. Popper, S. S. Waldstein and P. B. Szanto.—p. 724.
Artefacts in Liver Biopsies. T. C. Keller and H. F. Smetana.—p. 738.
*Acute Pancreatic Necrosis: Clinicopathologic Study. N. J. Roberts, A. H. Baggenstoss and M. W. Comfort.—p. 742.
Effect of Venous Compression on Certain Blood Factors. T. J. Berry, E. Perkins and P. Jernstrom.—p. 765.

Biopsy in Cirrhosis of Liver.—Popper and co-workers correlated clinical and laboratory observations with various histopathological features, such as liver cell damage, coagulation necrosis, fatty metamorphosis, focal necrosis and leukocytic reactions, in 97 liver biopsy specimens, obtained from 70 patients with cirrhosis. Diffuse liver cell damage showed the best correlation with clinical and with biochemical activity. The other features showed less correlation, which, when observed, was best explained by the concomitant presence of liver cell damage. This suggests that liver cell damage is the most important factor in determining the clinical activity in cirrhosis. A series of hepatic tests was performed on all patients within 48 hours to seven days of the biopsy. Increased cephalin flocculation and thymol turbidity tests appeared best to indicate the presence of diffuse liver cell damage in cirrhosis. These were followed by serum albumin reduction and to a lesser degree by serum globulin elevation and reduction of albumin-globulin ratio. Patients with an alcoholic history revealed, in general, less liver cell damage and more fatty metamorphosis than those without such a history. Ascites coincided most with scarring and other phenomena associated with fibroplasia and inflammation in the portal triads and in the connective tissue trabeculae. The type of cirrhosis associated with jaundice failed to reveal specific morphological characteristics except for the presence of static bile pigment. The morphological analysis did not reveal a structural basis for the pronounced jaundice or for the intrahepatic interruption of the biliary flow in cirrhosis.

Acute Pancreatic Necrosis.—Roberts and co-workers analyzed the clinical records and postmortem observations in 25 fatal cases of acute pancreatic necrosis in 13 men and 12 women between the ages of 26 and 73 years. The average age of the patients was 51.9 years. Sixteen patients, 11 women and five men, were described as obese. A record of the past consumption of alcohol was available in 10 patients, two of whom admitted excessive drinking and two others moderate drinking. No common causative denominator was immediately apparent. Most impressive was the coincidence of proved disease of the biliary tract in 21 of the 23 patients in which a description of the gross appearance of the biliary tract was available. Eighteen of these 23 patients had biliary stones. The disease occurs in both sexes and is most frequent in middle life. It is especially common in the obese and in alcoholics and often is precipitated after a meal or an alcoholic debauch. Its onset is usually sudden with severe constant upper abdominal pain, often extending to the back. Ordinarily the pain persists for at least several hours and often is not relieved by the usual doses of narcotics. Nausea and vomiting commonly occur promptly. A subnormal to normal temperature, low pulse rate and normal blood pressure are noted initially in most instances. Shock may develop early, late or not at all. Moderate to pronounced epigastric tenderness with only slight to moderate rigidity is usual. Subsequent distention is common and jaundice frequent. Conclusive laboratory assistance may be obtained by the demonstration of elevated serum levels of amylase and lipase in almost all cases observed early. Albuminuria is noted in most patients; sugar levels up to 20 per cent have been noted. Diagnosis, formerly difficult, is possible in most cases as a result of increased knowledge and awareness of the disease, coupled with the substantiating laboratory procedures now available.

American Journal of Ophthalmology, Chicago

33:1187-1324 (Aug.) 1950

Diabetic Retinopathy. J. S. Friedenwald.—p. 1187.
New Procedure for Treatment of Adherent Leukomas Preceding Keratoplasty. L. Paufique.—p. 1200.
Epibulbar Tumor. J. E. Ash.—p. 1203.
Ewing's Tumor of Orbit: Report of 2 Cases. F. Harbert and G. L. Tabor Jr.—p. 1219.
Streptothrix as Cause of Follicular Conjunctivitis and Other Obscure Conjunctivitides. F. H. Theodore.—p. 1225.
*Effect of ACTH in Glaucoma. E. M. Blake, R. M. Fasanella and A. S. Wong.—p. 1231.
Sutured Contact Lenses for Contention of Graft in Keratoplasty. A. Fritz.—p. 1236.
Nondiabetic Lipemia Retinalis. J. J. Groom and C. W. Rucker.—p. 1238.
Effects of Nicrowave Diathermy on Eye: Experimental Study. L. Daily Jr., K. G. Wakim, J. F. Herrick and others.—p. 1241.
Toxoplasmosis: Diagnosis and Treatment. A. B. Sabin.—p. 1255.
Plastic Socket and Lid Reconstruction. C. P. Scarborough and P. H. Landers.—p. 1269.
Presbyopia: Comparative Observations of White and Negro Populations. L. L. Covell.—p. 1275.
Abducens Paralysis in Brucellosis: Report of 2 Cases. J. C. Yaskin and R. S. Boles.—p. 1277.
Effect of Eye Patch on Organisms of Conjunctival Sac. R. W. Linhart. —p. 1280.

Effect of ACTH in Glaucoma.—Blake and his associates state that pituitary adrenocorticotropic hormone (ACTH) had no appreciable effect on the intraocular pressure in their first two cases of primary glaucoma. In the third patient uveitis in one eye appeared to be developing into primary bilateral glaucoma. Here the acutely raised tension and inflammation responded promptly in the one eye. The fourth patient who had early uveitis with a secondary rise in tension experienced a remarkable clinical improvement within 48 hours, including a definite drop in tension. The fifth case was one of chronic primary glaucoma, which, after eight days of treatment, showed no significant drop in pressure. It would appear that pituitary adrenocorticotropic hormone had no demonstrable effect in the reduction of intraocular pressure in primary glaucoma. Since increased intraocular pressure accompanying anterior uveal disease showed a drop in tension and subsidence of the inflammatory process, it is suggested that, if pituitary adrenocorticotropic hormone becomes more readily available, it may be useful in the differentiation between primary and so-called secondary glaucoma.

American Journal of Psychotherapy, New York

4:405-588 (July) 1950. **Partial Index**

SYMPOSIUM ON PROBLEM OF MEDICAL AND LAY PSYCHOTHERAPY

Medical View. I. Galdston.—p. 419.

Who Shall Practice Psychotherapy? R. M. Lindner.—p. 432.

Why Patients Discontinue Treatment in Mental Hygiene Clinic. E. Dengrove and S. B. Kutash.—p. 457.

Clinical Significance of Mosaic and Rorschach Methods. L. Zucker.—p. 473.

Polarity in Diagnosis Through Art. E. Zierer.—p. 488.

Archives of Dermatology and Syphilology, Chicago

62:181-350 (Aug.) 1950

Lesions of Scalp in Certain Scaly Dermatoses: Histologic Study. C. W. Laymon.—p. 181.

*Comparison of Muscle Biopsies and Bone Marrow Examinations in Dermatomyositis and Lupus Erythematosus. J. F. Madden and I. M. Karon.—p. 192.

Poikiloderma Vasculare Atrophicans: Report of Case Due to Exposure to Cold. J. G. Downing and J. M. Edelstein.—p. 206.

Beryllium Window Radiations for Superficial Therapy. A. C. Cipollaro.—p. 214.

Absorption of Roentgen Rays with Use of Beryllium Window Tube. M. F. Engman Jr., E. P. Weber and W. G. Elle.—p. 222.

Outcome of Pregnancies of Women Treated with Aqueous Penicillin for Early Infectious Syphilis: Prevention of Prenatal Syphilis. H. N. Bundesen, J. Rodriquez, H. C. S. Aron and B. F. Korman.—p. 230.

Shielding of Skin Against Roentgen Radiation by Plastic Compounds. J. W. Wilson.—p. 237.

Dermatologic Aspects of Insect Repellents and Toxicants. L. Goldman.—p. 245.

*Streptomycin Treatment of Granuloma Inguinale. H. Pariser, S. Z. Goldberg and G. H. Mitchell.—p. 261.

Effect of Yeast Extract on Microsporum Audouini and Microsporum Canis. K. Loewenthal.—p. 265.

*Chemosurgical Treatment of Melanoma: Microscopically Controlled Method of Excision. F. E. Mohs.—p. 269.

Peculiar Deformity of Hands Occurring in Epidermolysis Bullosa. M. H. Cohen and H. H. Hopkins.—p. 280.

Treatment of Onychomycosis with Ammoniacal Silver Nitrate Solution. A. G. Franks and A. Sternberg.—p. 287.

Therapeutic Value of Chloramphenicol in Group of Dermatoses of Established or Questionable Virus Etiology. L. G. Beinhauer.—p. 290.

Blood Vessels of Skin in Chronic Venous Insufficiency: Clinical and Pathologic Study. M. H. Kulwin and E. A. Hines Jr.—p. 293.

Atypical Keratosis Pilaris. F. P. Coombs and T. Butterworth.—p. 305.

Hypoallergenic Penicillin in Oil. S. W. Simon and M. D. Feldman.—p. 314.

Influence of Grenz Rays on Histamine-Induced Manifestations. G. Bucky, F. Blank and I. H. Distelheim.—p. 319.

Dermatomyositis and Lupus Erythematosus.—The difficulty encountered in differentiating acute disseminated lupus erythematosus from dermatomyositis prompted Madden and Karon to evaluate muscle biopsies done on patients with these diseases, and, because Hargraves found the so-called L. E. cell in bone marrow preparations from patients with acute disseminated lupus erythematosus, they also searched for such cells. The authors compare and correlate observations made on 27 patients, eight of whom had dermatomyositis and 19 of whom had lupus erythematosus. The 12 biopsies done on eight patients with dermatomyositis showed varying degrees of nodular myositis. The myositis was severer in the acute cases and decreased in intensity as the disease became chronic. Nodular myositis was seen in only six of 21 biopsy specimens from patients with lupus erythematosus. The myositis was severe in only one patient, who also had rheumatic fever, and mild in the other patients, who also had arthralgia, rheumatic pains or rheumatoid arthritis. Nodular myositis was not seen in a single case of lupus erythematosus that was not associated with rheumatic fever, arthralgia, rheumatic pains or arthritis. Nodular myositis was not seen in chronic or subacute lupus erythematosus. Degenerative processes in muscles appeared in all except one patient with dermatomyositis, but in only six of 19 cases of lupus erythematosus. Degenerative processes in muscles by themselves are of little assistance in diagnosis. Twenty-one sternal bone marrow examinations with special reference to L. E. cells were made in five cases of dermatomyositis, eight cases of acute disseminated lupus erythematosus and six cases of subacute lupus erythematosus. L. E. cells were not found in the bone marrow of patients with dermatomyositis or subacute or chronic lupus erythematosus, and they were found in only half the patients with acute disseminated lupus erythematosus. The L. E. cells are a valuable diagnostic aid, especially in cases of acute disseminated lupus erythematosus without cutaneous manifestation. Bone marrow examinations and muscle biopsies should be an aid in making the differentiation between dermatomyositis and lupus erythematosus.

Streptomycin in Granuloma Inguinale.—Pariser and his associates present observations on 76 patients with granuloma inguinale who were treated with streptomycin. The lesions of 80 per cent of their patients healed with a dosage of 18 Gm. of streptomycin given orally in divided doses of 0.6 Gm. every four hours over a five day period. Treatment failures could be reduced to approximately 4 per cent by retreatment with 4 Gm. per day over a period of 10 days. Although the oral use of aureomycin and chloramphenicol may cause healing of lesions resistant to intensive therapy with streptomycin, the experience of these authors with the drugs is too limited to permit one to draw conclusions.

Chemosurgical Treatment of Melanoma.—Mohs points out that in the treatment of epithelioma the "silent" extensions from the main mass of cancer can be traced and eradicated by means of multiple, microscopically controlled excisions which characterize the chemosurgical method. In the treatment of melanoma, however, this microscopic control would seem to be of more limited value, because often there is a discontinuous, embolic mode of spread into the peritumoral lymphatics and beyond. The author analyzes results obtained with his chemosurgical method in 20 patients with melanoma who have been observed for five or more years or until death. The primary melanoma was more than 3 cm. in diameter in 10 of the patients; 12 of the patients had received surgical or radiation treatment before the chemosurgical method was applied, and 10 had palpable enlargement of the lymph nodes at the time chemosurgical treatment was instituted. Seven of the 20 patients survived and were well for more than five years after treatment; one of them for more than 12 years. Nine of the remaining 13 patients died as the result of metastases; the other four died of either undetermined causes, "stroke" or pneumonia. These results compare favorably with those obtained by others using more radical methods. The chemosurgical method completely removes cutaneous melanomas. It is necessary to remove an additional zone of tissue after a melanoma-free level has been reached, because of the danger of satellite deposits in the surrounding lymphatics. The width of this extra zone varies in proportion to the size and the malignancy of the melanoma. The regional nodes are surgically dissected if enlarged or if the size and degree of malignancy of the primary lesion warrant a prophylactic dissection of nonpalpable nodes.

Archives of Pathology, Chicago

50:137-258 (Aug.) 1950

Hypertensive Cardiovascular Disease ("Malignant Hypertension"): Changes in Canine Tissues Induced by Various Manipulations of Kidney, with Special Reference to Vascular and Myocardial Lesions. E. E. Muirhead, A. Grollman and J. Vanatta.—p. 137.

*Crystalline Ester Cholesterol and Adult Cortical Renal Tumors. T. Leary.—p. 151.

Evaluation of Choline in Prevention of Experimental Atherosclerosis: Importance of Changes in Body Weight. C. Moses and G. M. Langabaugh.—p. 179.

Thickness of Media of Thoracic Aorta in Relation to Age. W. E. Wellman and J. E. Edwards.—p. 183.

Coronary Artery Disease: Comparison of Rates and Patterns of Development of Coronary Arteriosclerosis in Negro and White Races with Its Relation to Clinical Coronary Artery Disease. J. O. Blache and F. P. Handler.—p. 189.

Trichoma: Tumor of Hair Anlage. S. A. Wallace and B. Halpert.—p. 199.

Skeletal Changes in Severe Phosphorus Deficiency of Rat: I. Tibia, Metacarpal Bone, Costochondral Junction, Caudal Vertebra. R. D. Coleman, H. Becks, F. Van N. Kohl and D. H. Copp.—p. 209.

Changes Induced in Connective Tissue of Pubic Symphysis of Guinea Pig with Estrogen and Relaxin. E. Perl and H. R. Catchpole.—p. 233.

Arteritis of Appendix. J. W. Hall, S.-C. Sun and W. Mackler.—p. 240.

Crystalline Ester Cholesterol and Cortical Renal Tumors.—In this extensive discussion on cholesterol and the renal cortex, Leary pays particular attention to the relation of crystalline ester cholesterol to the cortical renal tumors occurring in adults. Miniature tumors were collected at the Mallory Institute of Pathology over a period of years. Solitary growths, nodules appearing in small numbers and, particularly, kidneys showing large numbers of nodules were studied. Evidence is presented that the crystalline ester cholesterol deposited in the

epithelium of renal convoluted tubules in adults, particularly in those afflicted with nephrosclerosis, is the stimulating agent responsible for the growth of benign cortical adenomas in man. Removal of the crystalline ester cholesterol is followed by a cessation of the growth of such adenomas, which then revert to inactive tubular adenomas. It is generally accepted that adult renal cortical adenocarcinomas have their origin in benign adenomas. Recent experimental chemical studies support the thesis that cholesterol by itself or in combination with small amounts of a cocarcinogen is the cause of sarcoma induced in mice by the injection of cholesterol-rich extracts of human or animal tissue. The combined histochemical and chemical evidence leaves little doubt that cholesterol is intimately related to certain human and experimental tumors.

Archives of Surgery, Chicago

61:193-386 (Aug.) 1950

Surgical Treatment of Chronic Suppurative Hidradenitis. P. W. Greeley. —p. 193.
Surgery of Gallbladder: Study of Results of Surgical Treatment in Rock County, Wis. T. J. Snodgrass, W. A. Munn and T. H. Flarity. —p. 199.
Role of Tracheotomy in Postoperative Care of Patients Subjected to Esophagectomy. J. T. Reynolds, P. H. Holinger, A. H. Andrews Jr. and others.—p. 211.
Combined Abdominal and Right Thoracic Approach to Lesions of Esophagus. C. Mathewson Jr. and R. Cohn.—p. 229.
Partial Esophagogastrectomy in Treatment of Esophagogastric Varices. P. W. Schafer and C. F. Kittle.—p. 235.
Problems Associated with Surgery of Heart and Great Vessels: Technical Problems Encountered in Surgery for Congenital Abnormalities. E. H. Fell, B. M. Gasul and C. B. Davis Jr.—p. 244.
Id.: Anesthetic Problems in Children Undergoing Operations on Heart and Great Vessels. F. M. Grem.—p. 259.
*Surgical Treatment of Tuberculous Pericarditis. E. Holman.—p. 266.
Splenectomy for Traumatic Rupture with Intra-Abdominal Hemorrhage: Report of 101 Cases. R. V. Byrne.—p. 273.
*Role of Stellate Block in Various Intracranial Pathologic States. H. C. Naffziger and J. E. Adams.—p. 286.
Intracranial Aneurysms. C. H. Shelden, R. H. Pudenz and L. E. Brannon.—p. 294.
Excision of Skin in Radical Mastectomy. H. D. Cogswell.—p. 305.
Technic for Radical Mastectomy. W. E. Leighton.—p. 312.
Effects of Sympathectomy on Cerebral Circulation of Hypertensive Patients. H. A. Shenkin, J. H. Hafkenschiel and S. S. Kety.—p. 319.
Irradiation Necrosis of Head of Femur. J. T. MacDougall, A. Gibson and T. H. Williams.—p. 325.
Physiologic Observations on Patient with External Pancreatic Fistula. J. M. Miller and M. Ginsberg.—p. 346.
Carcinoma of Ampulla of Vater of Minute Size: Unsuspected Cause of Obstructive Jaundice. L. H. Kyle, H. J. Sparling Jr. and H. Jeghers. —p. 357.
Relief of Pain in Chronic Relapsing Pancreatitis by Unilateral Sympathectomy. A. Hurwitz and J. Gurwitz.—p. 372.
Treatment of Fractures with Long-Standing Osteomyelitis: Results of Use of Tibial Sliding Graft. P. Wallace.—p. 379.

Surgical Treatment of Tuberculous Pericarditis.—Holman points out that tuberculous pericarditis poses the twofold problem of controlling infection and of correcting the mechanical interference with the flow of blood. He reviews four cases of tuberculous pericarditis cured or greatly improved by pericardectomy. The disease is characterized by a prolonged course exhibiting in the acute stage chills, sweats, fever, rapid pulse rate, dyspnea, increased sedimentation rate, leukocytosis, anemia, pericardial friction rub and pericardial effusion sufficient at times to produce compression of the heart and the superior and inferior venae cavae as shown by increased venous pressure, by fluoroscopic absence of ventricular pulsations and by a reduced voltage in the QRS complex and inverted T waves in the electrocardiogram. Such effusion may persist or may subside as shown by a reduction in the size of the cardiac shadow. In two cases this disappearance of pericardial effusion took place within three weeks after complete bed rest but was followed promptly by signs of cardiac compression due to contracture of the inflamed and thickened pericardium. Pericardiectomy should be considered at the time of pericardial effusion, particularly if compression of the heart and the superior and inferior venae cavae is present. In a very ill patient with pericardial effusion such decompression might be best effected by removal of the left sixth costal cartilage for evacuation and drainage of the pericardium, followed at a second stage, 10 to 20 days later, by median sternotomy and radical pericardiectomy. Despite the improvement following the first operation, the second operation should be performed without fail. Radical pericardiectomy in the four cases reviewed here resulted in apparent cure in three and in progressive improvement in one. Primary healing occurred in all operative areas, despite the presence of tubercle bacilli in the diseased pericardium. The beneficient influence of streptomycin and penicillin on the results is conceded.

Stellate Block in Intracranial Pathologic States.—According to Naffziger and Adams it is probable that cerebral vasospasm may either initiate or contribute to such neurological disorders as hemiplegia, aphasia and hemianopsia. Realizing this possibility, Leriche and Fontaine proposed interruption of the intracranial vascular sympathetic innervation by procaine hydrochloride block of the stellate ganglion. The improvement following stellate block in a patient with complete hemiplegia induced Naffziger and Adams to use this method in similar cases. They were reluctant to block the stellate ganglion when history or presence of blood in the cerebrospinal fluid indicated an acute cerebral hemorrhage, fearing that the bleeding might be augmented and the brain damage increased. In such cases they waited until bleeding (bloody cerebrospinal fluid) had subsided. An anterior approach to the region of the stellate ganglion was used in all instances. Two to 3 cc. of 1 per cent procaine hydrochloride was injected. The number and frequency of injections varied depending on the condition of the patient and the result obtained with the initial injection. One or two injections sufficed in many patients. Others required injection as often as three times daily for several days. Of the 155 patients with cerebrovascular accidents who were treated with stellate block, 91 made a complete clinical recovery, 37 made a partial recovery and in the remaining 27 the results were poor, in that they showed no improvement or died. Stellate block was employed also in 70 patients with acute neurologic deficits associated with trauma or intracranial operations. The results in these 70 patients without cerebrovascular disorders were good in 30, fair in 30 and poor in 10. The procedure has been extended to patients with neurological defects remaining as a result of prior cerebrovascular accidents. The authors observed improvement occurring as late as six years after the original vascular insult.

Arizona Medicine, Phoenix

7:1-64 (Aug.) 1950

Congenital Anteversion of Neck of Femur. R. S. Haines.—p. 19.
Diabetic Coma. E. A. Waskow.—p. 24.
*Use of Continuous Caudal or Spinal Anesthesia in Treatment of Eclampsia. R. B. Kennedy, L. Fill and R. R. Bates.—p. 27.

Continuous Caudal or Spinal Anesthesia in Treatment of Eclampsia.—Kennedy and his associates report the histories of four patients with eclamptogenic toxemia of pregnancy who were treated with continuous caudal and/or continuous spinal anesthesia supplemented by routine conservative medical management. In two of the cases the convulsive seizures occurred before delivery, while in the other two they occurred during the immediate postpartum period. One patient was treated by continuous caudal, one by continuous caudal later replaced by continuous spinal and two by continuous spinal anesthesia. The minimal length of time a patient was kept under continuous anesthesia was 13 hours, while the longest administration was 96 hours. Piperocaine hydrochloride was the anesthetic agent used in all cases except one, in which tetracaine hydrochloride was employed for a short time. The minimal caudal dose was 1,125 mg. and the maximal 3,525 mg.; the minimal dosage under continuous spinal was 622.5 mg. and the maximal 3,810 mg. Two patients responded with diuresis and alleviation of proteinuria within 12 hours after institution of therapy, while in the other two cases improvement was not definitely assured until 24 to 36 hours later. Three patients showed a definite decrease in hypertension during therapy; only one failed to show the drop in blood pressure shown by the others. Two patients were discharged with blood pressures slightly exceeding the arbitrary standards of 140/90. The authors used this treatment successfully in a large number of patients with preeclampsia and in many pregnant women with hypertensive cardiovascular disease. They do not wish to imply that this treatment will cure all eclamptic patients, but in their experience it is the best treatment available at the present time. They warn that this type of anesthesia is a powerful but dangerous therapeutic measure and should be used only by physicians thoroughly trained in its administration.

Arkansas Medical Society Journal, Fort Smith

47:55-70 (Aug.) 1950

Medical Ethics: Your Own Course in Curriculum. H. A. Kemp.—p. 55.
No Apologia. J. P. Sanders.—p. 59.

Bulletin New York Academy of Medicine, New York

26:583-636 (Sept.) 1950

Comparison of Tests of Thyroid Function. J. H. Means.—p. 583.
Thyrotropic Exophthalmos. R. L. Pfeiffer.—p. 592.
Diabetic Neuropathy. R. W. Rundles.—p. 598.
Advances in the Diagnosis of Bacterial Infections. G. Shwartzman. —p. 617.

Canadian Medical Association Journal, Montreal

63:103-210 (Aug.) 1950

Exfoliative Cytological Diagnosis. D. Magner.—p. 103.
Physiological Factors of Significance in Paediatric Anaesthesia. C. R. Stephen.—p. 109.
Primary or Idiopathic Pleurisy with Effusion. W. A. Oille.—p. 112.
Needle Biopsy of Liver. I. D. Maxwell, M. M. Baird and M. V. Rae. —p. 116.
*Rheumatoid Arthritis: Results of Treatment with Desoxycorticosterone Acetate and Ascorbic Acid (Arthrodox). W. Graham, T. E. Hunt and D. Mowat.—p. 121.
Flaxedil, New Curarizing Agent. F. A. Walton.—p. 123.
*Convulsions and Hemiplegia in Pertussis Prophylaxis. H. B. Grace. —p. 129.
Friedlander's Bacillus Meningitis. C. W. Holland.—p. 131.
Early Symptomatology of Carcinoma of Lung. B. Winter.—p. 134.
Neurological Complications of Infectious Mononucleosis. J. L. Silversides and J. C. Richardson.—p. 138.
Pulmonary Calcification and Histoplasmin Sensitivity. P. Green.—p. 143.
Failure After Operations for Procidentia Uteri. N. M. Gulon.—p. 147.
Giant Follicular Hyperplasia of Rectum Showing Malignant Degeneration. D. J. Currie and J. C. Luke.—p. 150.
Adrenal Neuroblastoma. R. W. Boyd.—p. 153.
Multiple Myeloma. E. G. Brownell.—p. 157.
Hyperglycaemic and Glycogenolytic Factor of Pancreas. E. Lozinski. —p. 163.

Desoxycorticosterone Acetate and Ascorbic Acid in Rheumatoid Arthritis.—Graham, Hunt and Mowat point out that Lewin and Wassén reported that in a majority of patients with rheumatoid arthritis a dramatic decrease in pain and stiffness followed the parenteral administration of desoxycorticosterone acetate and ascorbic acid. Ten subsequent reports have given rise to controversy since five of them seemed to confirm the observations of Lewin and Wassén whereas the others, with the same technic employed, reported no significant response. Graham and his associates describe their observations on 37 patients with rheumatoid arthritis, 10 with ankylosing (Marie-Strümpell) spondylitis and three with acute gouty arthritis who were treated with intramuscular administration of desoxycorticosterone acetate and ascorbic acid combined. Treatment was continued for one to 14 days. In most of the patients no obvious change, subjective or objective, was noted. A few, however, described temporary, sometimes dramatic, relief from stiffness and pain, especially after the first injection. In view of the psychological factors involved, such temporary improvement must be interpreted with caution. Treatment with desoxycorticosterone acetate and ascorbic acid was found to have no effect on the activity or the progression of the diseases as shown by the degree of swelling, the erythrocyte sedimentation rate and serum protein fractions. The injection of desoxycorticosterone acetate and ascorbic acid did not have any effect on the total circulating eosinophil counts or glucose tolerance curves, such as are found after therapy with cortisone or pituitary adrenocorticotropic hormone.

Convulsions and Hemiplegia in Prophylaxis of Pertussis.—Grace describes two cases in which severe untoward reactions followed administration of multiple antigens for prophylactic immunization. The preparation used was a fluid form of diphtheria toxoid, pertussis vaccine and tetanus toxoid (combined). The dose given was 0.5 cc. which contained approximately 11,250,000,000 killed bacilli from strains in phase I Hemophilus pertussis, 15 L.F.D. of diphtheria toxoid and 5 L.F.D. of tetanus toxoid. The pertussis component of the preparation is considered responsible for the adverse effects produced. In the first case an explosive episode occurred with severe prolonged convulsive seizure and right-sided hemiplegia. Sequelae remain which are indicative of permanent cerebral damage. In the second case the reaction was less violent; complete recovery followed the convulsive seizure. The authors cite other reports of similar untoward effects occurring with pertussis preparations of various types alone or in combinations with other antigens and manufactured by different companies. They direct attention to the serious results which may occur when pertussis antigen is administered to a subject who is predisposed to the convulsive state.

Cancer Research, Chicago

10:461-522 (Aug.) 1950

Recent Studies on Corneal Metabolism and Growth: Review. J. S. Friedenwald.—p. 461.
Studies on Hodgkin's Syndrome: XI. Influence of Normal Serum and Hodgkin's Serum on Cellular Growth and Morphology in Tissue Culture. M. S. Reiman, I. R. Stern, M. Z. Ford and H. A. Hoster. —p. 467.
Virus-Induced Rabbit Papilloma-to-Carcinoma Sequence: III. Immunological Tests for Papilloma Virus in Cottontail Carcinomas. J. T. Syverton, E. B. Wells, J. Koonin jr. and others.—p. 474.
Significance of Anterior Chamber in Tumor Transplantation: I. Transplantation of Mouse Neuroblastoma C1300 to Homologous Hosts. E. J. Eichwald, R. G. Evans and G. B. Browning.—p. 483.
Studies on Xanthine Oxidase During Carcinogenesis by p-Dimethylaminoazobenzene. W. W. Westerfeld, D. A. Richert and M. F. Hilfinger. —p. 486.
Application of Seibert Tryptophane-Acid Reaction to Serum of Malignancy. C. Riegel and P. R. Beatty.—p. 495.
Catalase Studies on Normal and Cancerous Rats. D. Appleman, E. R. Skavinski and A. M. Stein.—p. 498.
Studies of Excretion of Diazotizable Material After Feeding 2-Acetylaminofluorene to Rats. H. P. Morris and B. B. Westfall.—p. 506.
Inhibition of Nucleic Acid Synthesis by Folic Acid Antagonists. H. E. Skipper, J. H. Mitchell Jr. and L. L. Bennett Jr.—p. 510.
Relative Susceptibility of Various Organs to Tumor Transplantation. R. P. de Long and D. R. Coman.—p. 513.
Titration of Milk Agent Virus in Milk and Lactating Mammary Gland Cells. R. A. Huseby, C. P. Barnum and J. J. Bittner.—p. 516.

Connecticut State Medical Journal, Hartford

14:687-806 (Aug.) 1950

*Blue Cross Protects the People—Who Protects Blue Cross? P. R. Hawley.—p. 687.
Need for Standardization of Breast Cancer Records. R. Katzenstein, R. J. Kerin and A. J. Ryan.—p. 692.
Unsuspected Foreign Body of Bronchus—Case Report. F. M. Bannon. —p. 696.
Clinical Value of Electrocardiography. M. Backer.—p. 699.
Lipectomy for Abdominal Fat. C. L. Larkin.—p. 706.
Retrocaval Ureter—Case Report. C. E. Jacobson Jr.—p. 709.
Diabetics Live Long, but Can Live Longer and More Efficiently. E. P. Joslin.—p. 713.

Who Protects Blue Cross?—Howley feels that the medical profession has been slow to realize that in its hands, almost exclusively, rests the success of voluntary prepayment of the costs of medical care. Blue Cross has been caught between the upper and nether millstones of spiraling costs and increasing utilization. As the utilization rate rises, the subscribers must pay more, and the day may come when Blue Cross will be too expensive for poor people; when that day comes, there will be compulsory health insurance. Hawley pleads that Blue Cross be protected against being priced out of the market. He suggests among other factors elimination of services which are purely luxuries and which do not contribute significantly to the recovery of patients. Hospital administrators and pathologists must bring to the attention of the staff as a whole the unnecessary services that are being ordered for patients. The author deplores the curious defect in public morality which makes it no crime to defraud an insurance company. Many persons who would be horrified at the thought of stealing one penny from a fellow man have not the slightest compunction about taking money under false pretenses from an insurance company. Patients may demand hospitalization as a luxury rather than as a necessity. On the excuse that the home is being renovated or that the cook will not return for several days, the patient may ask to remain in the hospital beyond the time that hospital care is necessary. It is not easy for the physician to pit his own sense of right and wrong against a patient's capricious desire. It should be made easier for him by Blue Cross members' awareness that each day of unnecessary utilization of their benefits must be paid for by increased cost of their own protection as well as that of all other Blue Cross members.

Diseases of Chest, Chicago

18:93-184 (Aug.) 1950

Use of PAS in Treatment of Draining Tuberculous Empyemata. M. R. Lichtenstein and P. Alfano.—p. 93.
Endoscopic Collection of Neoplastic Cells and Tubercle Bacilli from Bronchi (Description of New Irrigation-Suction Collector and Anatomical, Physiological, and Pathologic Factors Involved). A. A. Carabelli.—p. 98.
Significance of Unstable Tuberculin Reactions. I. S. Neiman.—p. 111.
Pulmonary Diseases Service Rehabilitation Program of Veterans Administration Hospital. J. D. Davis and C. W. Anderson.—p. 119.
*Shrunken Right Middle Lobe with Reference to So-Called "Middle Lobe Syndrome." E. H. Rubin and M. Rubin.—p. 127.
Experimental Massive Pulmonary Collapse. W. W. Coulter Jr.—p. 146.
Benign Thymic Cyst: Case Report. J. A. Crellin, T. F. Pugh and O. H. Janton Jr.—p. 154.
Metastatic Malignant Tumors to Bronchus Found in Bronchial Biopsy and Secretions. I. M. Reingold and B. E. Konwaler.—p. 162.
Autopsy Incidence of Pulmonary Embolism in Tuberculosis. T. J. Moran.—p. 171.

Shrunken Right Middle Lobe.—The Rubins report on 16 patients with a shrunken right middle lobe, a condition referred to by some as the "middle lobe syndrome." The right middle lobe is most subject to collapse. This is due to the fact that its bronchus is especially vulnerable to compression and invasion by bronchopulmonary lymph nodes, the latter draining the lower as well as the middle lobe. It is possible that middle lobe shrinkage occurs as a result of pressure exerted on bronchi by cicatrizing nontuberculous lymph nodes, but the analysis of the histories and roentgen observations in these 16 cases suggest that in each instance a preexisting tuberculous focus, probably in regional lymph nodes, led to the involvement of the middle lobe. The symptoms produced by the shrunken middle lobe are usually like those of bronchitis, but there are intercurrent episodes of pulmonary infections or hemoptysis. Usually the course is mild. The true cause may be overlooked or the symptoms erroneously ascribed to pleuropericardial adhesions or interlobar pleurisy. The diagnosis can be made by roentgenography in the posteroanterior, right lateral and lordotic projections. The shrunken lobe appears as a triangular or roughly quadrilateral density at the root of the lung. Tomography is helpful. Bronchoscopy is essential in the determination as to whether one is dealing with bronchiogenic neoplasm. Bronchography is necessary for establishment of the presence of bronchiectasis. Treatment consists of excision of the involved lobe unless the age and condition of the patient contraindicate surgery.

Florida Medical Association Journal, Jacksonville

37:1-60 (July) 1950. **Partial Index**

Shock Therapy Comes of Age. W. H. McConnell.—p. 19.
General Practitioner's Care of Prostate. A. F. Turner Jr.—p. 27.
Multiple Small Bowel Intussusception. N. Arenson.—p. 31.

37:61-120 (Aug.) 1950

Venous Thrombosis. A. Ochsner, M. E. DeBakey and P. T. DeCamp.—p. 79.
Treatment of Pelvic Malignant Disease. E. Novak.—p. 83.
*Visual and Retinal Complications of Diabetes Mellitus. W. J. Knauer.—p. 88.
*Granuloma of Larynx Following Intratracheal Anesthesia. M. Wattles.—p. 91.
6n Propyl Thiouracil in Thyrotoxicosis Complicating Pregnancy. M. S. Saslaw and H. Kraff.—p. 94.

Visual Complications of Diabetes Mellitus.—Knauer says that, as the life of diabetic patients is prolonged, diabetes mellitus may top the list of causes of loss of vision. At least 40 per cent of patients who have had diabetes mellitus for 15 years will have some form of retinopathy. The percentage rises to 85 for the group who have had this disease for 25 years or more. Ophthalmologists should record the time at which diabetes mellitus was first diagnosed in cases of diabetic retinopathy. The patients should be told to report visual disturbances. The diabetic changes in the retina, which are usually bilateral, occur in the area between the upper and lower temporal vessels and the region surrounding the optic nerve head. Numerous so-called small round deeply situated hemorrhages or hemorrhagic spots occur, and, in addition, there are usually small exudates. Treatment with rutin seems to improve the capillary fragility but not the diabetic retinal lesions. The hope that early and physiological control of the diabetes may avert later hopeless and disastrous complications is gaining ground. By close cooperation between the internist and the ophthalmologist it may be possible to evolve a method whereby retinal complications can be avoided and blindness from diabetes eliminated. The author stresses that patients who have had diabetes mellitus for 10 years or more should undergo ocular examination at regular and relatively frequent intervals and the fundus of the eye should be carefully examined.

Granuloma of Larynx Following Intratracheal Anesthesia.—Wattles believes that granuloma of the larynx following intratracheal anesthesia is more frequent than the few reported cases seem to indicate. Of the 22 cases that had been recorded to the end of September 1949 more than three fourths (17) were in women. The favored site appears to be the posterior portion of the vocal cord or on or near the vocal process of the arytenoid cartilage, where the lesion is subject to trauma in the use of the voice. Chronic nonspecific inflammation characterizes the condition. There may be polypoid masses composed of new granulation tissue richly supplied with blood vessels and covered with inflammatory exudate or small, hard, fibrous nodules composed of inflammatory fibrous tissue with few blood vessels, the whole covered with epithelium. Granulation tissue may surround the cartilage of the vocal process; the cartilage may be found in the floor of the ulcer or may be loose in the granuloma. The cause is obviously mechanical. The intratracheal tube, by pressure necrosis or trauma, produces an ulcer of the larynx. The chief symptom is hoarseness. Other complaints are discomfort in the larynx, pain extending to the ear and occasionally hemoptysis and chronic cough. Dyspnea and cyanosis may make an emergency operation necessary. Treatment consists of removal of the granuloma. Recurrence of the granuloma may require repeated excision. The lesion frequently occurs bilaterally, as in the case which the author observed. Every effort should be made to avoid this complication through gentleness during intubation, careful examination of the larynx preoperatively and postoperatively and appropriate treatment of abrasions. Surgeons should be aware of this possible complication, and, when a patient, particularly a woman, complains of hoarseness, loss of voice, laryngeal pain or discomfort in the throat after tracheal intubation, the larynx should be examined with this sequela in mind.

Gastroenterology, Baltimore

15:581-814 (Aug.) 1950

Psychosomatic Relationships in Digestive System. J. A. Bargen.—p. 581.
Review of Gastric Surgery for 1948. S. F. Marshall and E. S. Phillips Jr.—p. 592.
Studies in Pancreatic Function: II. Statistical Study of Pancreatic Secretion Following Secretin in Patients Without Pancreatic Disease. D. A. Dreiling and F. Hollander.—p. 620.
Flocculation Tests in Differential Diagnosis of Jaundice. H. Ducci.—p. 628.
Infectious Hepatitis (Homologous Serum Type) in Drug Addicts. F. Steigmann, S. Hymann and R. Goldbloom.—p. 642.
Hookworm Infection in Veterans, with Some Notes on Strongyloides Stercoralis and Other Parasites. H. C. Conn.—p. 647.
Occurrence of Proctologic Disorders in Infancy and Childhood: Statistical Review of 2700 Cases. S. Schapiro.—p. 653.
Changes in Gastroscopic Appearance of Human Stomach Following Intravenous Tetra-Ethyl Ammonium Chloride. A. Hendin, A. L. Hahn and W. A. Knight Jr.—p. 667.
Red Goggle Examination of Superficial Venous Collaterals: Simple Clinical Substitute for Infrared Photograph. A. P. Ingegno and B. F. Merrill.—p. 670.
Gallstone Ileus. V. R. Forester.—p. 679.
Carcinoma of Gallbladder. A. W. Ulin, I. L. Lichtenstein, A. Garritano and S. M. Fischer.—p. 684.
Lesser Peritoneal Sac Perforation Complicating Benign Peptic Ulcer. II. Clinical and Roentgenologic Study. M. Feldman.—p. 689.
Id.: III. Report of Two Cases. M. Feldman and T. Weinberg.—p. 696.
Serum Amylase Response to Morphine, Mecholyl and Secretin as Test of Pancreatic Function. J. O. Burke, K. Plummer and S. Bradford.—p. 699.
Histological Investigation of Healing of Acute Gastric Ulceration in Cat. G. S. Gunter.—p. 708.
Effect of Banthine on Gastric Secretion in Man and Experimental Animals. C. A. Smith, E. R. Woodward, C. W. Janes and L. R. Dragstedt.—p. 718.
Comparison of Effectiveness of Banthine and Atropine in Depressing Gastric Acid Secretion in Man and Dog. F. B. Benjamin, C. E. Rosiere and M. I. Grossman.—p. 727.
*Effect of Atropine on Certain Gastric Functions in Patients with Duodenal Ulcer. B. F. Gill and J. S. Jessup.—p. 736.

Effect of Atropine on Gastric Functions.—Gill and Jessup describe studies made on six hospitalized male patients with uncomplicated duodenal ulcer in order to determine the effects on certain functions of the stomach of atropine sulfate

given by mouth. A dye dilution technic was employed to calculate the rates of gastric secretion and pyloric evacuation. Definite diminution in free and total acid production, rate of gastric secretion and rate of pyloric evacuation was observed while the patients were receiving atropine. These studies corroborate the generally held concept that the parasympathetic nervous system, through the vagus nerves, stimulates secretion and motility of the human stomach and that atropine is an effective inhibitor of this action. Results with atropine are similar to the immediate results of vagotomy. The large doses of atropine used in this study caused blurring of vision and dryness of the mouth. The fact that a dose of 2.4 mg. of atropine sulfate given every four hours produced no greater decrease in acid or motility than a dose of 1.2 mg. suggests that atropine in even smaller doses might be sufficient to obtain the desired results. Caution is advisable in the use of atropine in older patients with cardiovascular disease or increased intraocular tension.

Georgia Medical Association Journal, Atlanta

39:313-358 (Aug.) 1950

Today's Indications for Cesarean Section. M. M. Schneider.—p. 313.
Diagnosis of Obstructive Lesions of Gastrointestinal Tract of Newborn Infant. M. H. Roberts.—p. 320.
Diagnosis and Early Management of Acute Poliomyelitis. M. L. Davis.—p. 327.
Rehabilitation of the Crippled Child. H. E. Gillette.—p. 332.
Treatment of Flat Feet in Children. J. H. Kite and W. W. Lovell.—p. 335.

Journal of Clinical Investigation, Cincinnati

29:973-1112 (Aug.) 1950

*Salt Retention in Cirrhosis of Liver. A. V. N. Goodyer, A. S. Relman, F. D. Lawrason and F. H. Epstein.—p. 973.
Comparative Absorption of Vitamin A from Water-Miscible and Oily Preparation by Normal Human Adults and Patients with Steatorrhea. B. C. Barnes, E. E. Wollaeger and H. L. Mason.—p. 982.
Transfer of Radioactive Mercury Across Membrane Produced by Application of Cantharides to Skin of Man. F. J. Kelly, A. H. Svedberg and V. C. Harp Jr.—p. 988.
Metabolic and Cardiovascular Studies of Prolonged Intravenous Administration of Human Serum Albumin. N. S. Gimbel, C. Riegel and W. W. L. Glenn.—p. 998.
Cerebral Circulation and Metabolism in Hyperthyroidism. P. Scheinberg.—p. 1010.
Studies in Para-Aminohippuric Acid Synthesis in Human: Its Application as Liver Function Test. W. P. Deiss and P. P. Cohen.—p. 1014.
Mechanism of Glycosuric Diuresis in Diabetic Man. W. A. Brodsky, S. Rapoport and C. D. West.—p. 1021.
Concentration of Precipitable Iodine in Serum. D. M. Kydd, E. B. Mann and J. P. Peters.—p. 1033.
Plasma and Red Cell Iron Turnover in Normal Subjects and in Patients Having Various Hematopoietic Disorders. R. L. Huff, T. G. Hennessy, R. E. Austin and others.—p. 1041.
Effect of Alcohol on Renal Excretion of Water and Electrolyte. M. B. Strauss, J. D. Rosenbaum and W. P. Nelson III.—p. 1053.
Studies on Proteolytic Enzyme System of Blood. II. Fibrinolysokinase Activators for Profibrinolysin. J. H. Lewis and J. H. Ferguson.—p. 1059.
Correlative Study of Cardiac Output and Hepatic Circulation in Hyperthyroidism. J. D. Myers, E. S. Brannon and B. C. Holland.—p. 1069.
*Iron Metabolism. Hematopoiesis Following Phlebotomy. Iron as Limiting Factor. S. Finch, D. Haskins and C. A. Finch.—p. 1078.
Mucolytic Enzyme Systems: X. Serum Hyaluronidase Inhibitor in Liver Disease. G. G. Snively and D. Glick.—p. 1087.
Position of Oxygen Dissociation Curve of Blood in Normal Children and Adults. M. Morse, D. E. Cassels and M. Holder.—p. 1091.
Position of Oxygen Dissociation Curve of Blood in Cyanotic Congenital Heart Disease. M. Morse, D. E. Cassels and M. Holder.—p. 1098.
Effect of Salicylates and Adrenocorticotropic Hormone upon Miscible Pool of Uric Acid in Gout. J. D. Benedict, P. H. Forsham, M. Roche and others.—p. 1104.

Salt Retention in Cirrhosis of Liver.—Goodyer and his associates infused 500 cc. of a 5 per cent solution of sodium chloride into normal adults and into patients with cirrhosis, most of whom had normal glomerular filtration rates and renal plasma flows. All subjects were deprived of food and water for 12 hours before the infusion and for six to eight hours thereafter. The concentrations of serum sodium rose about 10 milliequivalents per liter during the infusions in all experiments and remained elevated during the subsequent period of water deprivation, during which time the normal subjects and two patients with cirrhosis without ascites or edema excreted 12 to 54 per cent of the administered sodium. The concentration of sodium in their urine increased to as much as 267 milliequivalents per liter and the rate of sodium excretion increased greatly. In contrast, during the same period, the cirrhotic patients with edema and/or ascites excreted 0.2 to 10 per cent of the administered sodium. The concentration of sodium in their urine increased to a maximum of 102 milliequivalents per liter, and the rate of sodium excretion increased only minimally. Potassium excretion increased in most patients coincidentally with the sodium uresis. The authors regard the results of these tests as evidence of a specific impairment of the renal mechanism for the excretion of sodium in patients in whom hepatic cirrhosis is accompanied with edema and/or ascites. It appears that dietary sodium is retained by the kidneys of these patients as a result of the increased tubular reabsorption, the stimulus for which remains obscure.

Iron Metabolism: Hematopoiesis Following Phlebotomy.—In the studies reported by Finch and his associates, dogs and men were repeatedly subjected to phlebotomy over a period of several months. The bleeding produced anemia and thereby stimulated hematopoiesis. The removal of 3,500 cc. of blood in normal subjects over a period of seven weeks resulted in, first, an increased rate of blood formation and later, as iron depletion became manifest, a retardation of hematopoiesis. While on a normal diet without supplemental iron therapy, the subjects recovered from the anemia in two months. The serum iron level remained depressed, suggesting a deficiency in iron stores over a longer period. Hematopoiesis was severely curtailed in persons with depleted stores of iron. In patients with excessive tissue iron, including those with hemochromatosis, blood production continued at an accelerated rate. Weekly phlebotomies of 500 cc. could be continued for several months without the development of significant anemia. From data obtained on phlebotomized patients with polycythemia vera, the maximal amount of iron available from the diet for hemoglobin production seems to be 2 to 4 mg. per day. This would contribute but little to the total iron mobilized under the conditions of the experiment. These observations indicate that the rate of blood regeneration following phlebotomy is dependent chiefly on available body stores of iron.

Journal of Immunology, Baltimore

65:143-296 (Aug.) 1950

Combined Active-Passive Reimmunization Against Tetanus in Previously Immunized Individuals: Experimental and Clinical Evidence. J. J. Miller Jr. and M. L. Ryan.—p. 143.
Antigenic Relationships of Certain Viruses Capable of Producing Encephalitis in Mice: As Shown by Complement Fixation Tests. T. P. Hughes and A. Perlowagora.—p. 155.
Antigenic Relationships of Native Antigens of Species of Brucella. S. J. Silverman and S. S. Elberg.—p. 163.
New Method for Large-Scale Production of High-Titer Botulinum Formol-Toxoid Types C and D. M. Sterne and L. M. Wentzel.—p. 175.
Action of Aureomycin and Other Chemotherapeutic Agents in Experimental Brucellosis. A. I. Braude and W. W. Spink.—p. 185.
Interchangeability of Complement Components of Different Animal Species: II. In Hemolysis of Sheep Erythrocytes Sensitized with Rabbit Amboceptor. C. E. Rice and C. N. Crowson.—p. 201.
*Q Fever in California: II. Recovery of Coxiella Burneti from Naturally-Infected Air-Borne Dust. P. D. DeLay, E. H. Lennette and K. B. DeOme.—p. 211.
Differences in Toxicity of S- and R-Variants of Shigella Dysenteriae. Chloe Tal.—p. 221.
Comparison of Influenza Complement Fixation Antigens Derived from Allantoic Fluids and Membranes. M. W. Kirber and W. Henle.—p. 229.
Evaluation of Agglutination of Erythrocytes Sensitized by Newcastle Disease Virus (NDV) as Serologic Test in Infectious Mononucleosis. L. Kilham.—p. 245.
Comparison of Physicochemical Measurements of Hyaluronidase and of Neutralizing Antibodies Thereto. T. N. Harris and S. Harris.—p. 255.
Egg-White Inhibitor of Influenza Virus Hemagglutination: III. Stability in Relation to Preparation of Standard of Activity. F. Lanni, Y. T. Lanni and J. W. Beard.—p. 269.
Hemagglutinating Substances for Human Cells in Various Egyptian Plants. W. C. Boyd.—p. 281.
Electron Microscopy of Fowl Pox Virus Within Chorioallantoic Membrane. C. Morgan and R. W. G. Wyckoff.—p. 285.

Q Fever: Recovery of Coxiella Burnetii from Dust.—Coxiella burnetti, the causal organism of Q fever, was found in California in the milk of infected dairy cattle, sheep and goats. Many human cases of Q fever occurring in California could be tracted neither to the use of raw milk nor to contact with dairy cattle, sheep or goats. It is possible that infection may arise from air-borne dust originating in environments contaminated with the body secretions or excreta of infected livestock. This report presents data on initial experiments conducted

to ascertain the presence of Coxiella burnetii in dust from such environments. The authors recovered Coxiella burnetii from dust-laden air on a dairy in southern California and from dust-laden air on a sheep ranch in northern California. Thus it has been demonstrated that Coxiella burnetii may be present in the dust-laden air on premises harboring infected domestic livestock. The possibility thus exists that human (or animal) infection may be acquired by exposure to contaminated air. Air-borne dissemination of the rickettsiae might offer an explanation for some of the outbreaks and sporadic cases of Q fever which have occurred in the absence of direct contact with infected livestock.

Journal of International College of Surgeons, Chicago

14:143-256 (Aug.) 1950

Morbidity After Prostatectomy: Urethrocystographic Study. M. L. Brondy and S. A. Robins.—p. 143.
Clinical and Roentgenologic Manifestations of Obstruction of Small Bowel. C. J. Hunt.—p. 159.
Küntscher Nail Technic for Fractures of Femoral Shaft. J. E. M. Thomson.—p. 166.
Management of Urinary Incontinence in Women. W. J. Reich, J. L. Wilkey, M. J. Nechtow and H. E. Silverman.—p. 188.
Prevention of Some Post-Gastrectomy Difficulties by New Gastrectomy Technic (Pantaloon Anastomosis). M. E. Steinberg.—p. 194.
Primary Carcinoma of Duodenum: Report of Successful Whipple Operation. R. Goldsmith, S. Levine and J. Zaslow.—p. 205.
Unicornuate Uterus Associated with Agenesis of Kidney: Report of 2 Cases. A. F. Daro, H. A. Gollin and E. G. Nora Jr.—p. 211.
Study on Cause of Toxemia of Pregnancy. M. Magara.—p. 215.
Management of Acute Cholecystitis. A. Behrend.—p. 222.

Journal of Investigative Dermatology, Baltimore

15:69-156 (Aug.) 1950

Thorium-X Investigations: Histological Study of Thorium-X Application on Rabbit Skin. H. C. Fishman.—p. 71.
Cutaneous Sarcoidosis as Expression of Syphilis: Report and Discussion of Case. E. T. Bernstein and M. Leider.—p. 75.
Relationship of Host and Virus in Molluscum Contagiosum. G. Rake and H. Blank.—p. 81.
Etiology of Poral Closure: Experimental Study of Miliaria Rubra, Bullous Impetigo and Related Diseases of Skin: I. Historical Review of Causation of Miliaria. J. P. O'Brien.—p. 95.
Id.: II. Role of Staphylococcal Infection in Miliaria Rubra and Bullous Impetigo. J. P. O'Brien.—p. 102.
Id.: III. Pathologic Effect of Excessive Soaping on Pores of Skin. J. P. O'Brien.—p. 134.
Id.: IV. Effect of Lipoid Solvents on Pores of Skin. Final Discussion of Poral Closure. J. P. O'Brien.—p. 141.
Comments to "The Etiology of Poral Closure, an Experimental Study of Miliaria Rubra, Bullous Impetigo and Related Diseases of Skin. By John P. O'Brien, M.D." M. B. Sulzberger and F. Herrmann.—p. 153.

Journal Pharmacology & Exper. Therap., Baltimore

99:395-502 (Aug.) [Part I] 1950. **Partial Index**

Cardiac Action of Helleborus Glycosides and Their Aglycones. K. K. Chen, F. G. Henderson and R. C. Anderson.—p. 395.
Quantitative Study of Blood Pressure Response to Cardiovascular Drugs and Their Antagonists. G. Chen and D. Russell.—p. 401.
Physiological Disposition of Dicumarol in Man. M. Weiner, S. Shapiro, J. Axelrod and others.—p. 409.
Mechanism of Apnea Following Intravenous Injection of Various Antihistaminic Compounds; Its Relation to Their Chemical Structure. D. M. Aviado Jr., R. G. Pontius and T. H. Li.—p. 425.
Pharmacology of New Autonomic Ganglion Blocking Agent, 2,6-Dimethyl-1,1-Diethyl Piperidinium Bromide (SC-1950). D. L. Cook, W. E. Hambourger and R. G. Bianchi.—p. 435.
Potentiation of Antimalarial Activity of Sulfadiazine by 2,4-Diamino-5-Aryloxyprimidines. J. Greenberg and E. M. Richeson.—p. 444.
Toxicity, Antipyretic and Analgesic Studies on 39 Compounds, Including Aspirin, Phenacetin and 27 Derivatives of Carbazole and Tetrahydrocarbazole. E. Eagle and A. J. Carlson.—p. 450.
Choleretic Potencies of Some Synthetic Compounds. M. J. Gunter, K. S. Kim, D. F. Magee and others.—p. 465.

99:227-398 [Aug.] (Part II) 1950

Functional Characteristics of Renal Transport Mechanisms. K. H. Beyer.—p. 227.
Recent Contributions to Pharmacology of Bis(2-Haloethyl) Amines and Sulfides. F. S. Philips.—p. 281.
Carbon Monoxide. J. L. Lilienthal Jr.—p. 324.
*Addiction to Analgesics and Barbiturates. H. Isbell and H. F. Fraser.—p. 355.

Addiction to Analgesics and Barbiturates.—Isbell and Fraser review the literature of the last decade on addiction to analgesic drugs. They found that every drug in the morphine series which is an effective analgesic is also capable of producing addiction and that the likelihood of producing addiction generally parellels the analgesic potencies of the morphine drugs. Addiction to meperidine hydrochloride is fairly common, and physical dependence can be developed in persons who have never been previously addicted to any other analgesic drug. The spinal cord, and probably other parts of the central nervous system, are involved in physical dependence on morphine. This dependence is not entirely due to changes in the autonomic nervous system. Addiction to morphine and other analgesics causes a general slowing up of the electroencephalogram. No permanent anatomic damage is done to the central nervous system, nor is there permanent impairment of intelligence. Treatment of morphine addiction involves withdrawal of the drug followed by a long period of rehabilitative and psychiatric therapy. Addiction to barbiturates is far more dangerous and harmful than is addiction to morphine. The clinical picture of chronic barbiturate intoxication resembles that of chronic intoxication with alcohol and is characterized by impairment of mental ability, impairment of emotional control, psychic regression and dangerous neurological symptoms. Withdrawal of barbiturates is followed by a severe type of abstinence syndrome which is characterized by convulsions and delirium. Treatment of chronic barbiturate intoxication is the same as for morphine addiction.

Journal of Thoracic Surgery, St. Louis

20:169-334 (Aug.) 1950. **Partial Index**

Primary Intrathoracic Neurogenic Tumors. J. T. Godwin, W. L. Watson, J. L. Pool and others.—p. 169.
*Tumors of Thymus. W. D. Seybold, J. R. McDonald, O. T. Clagett and C. A. Good.—p. 195.
Syphilis of Esophagus. T. R. Hudson and J. R. Head.—p. 216.
*Cavernostomy for Residual Cavity After Thoracoplasty: Early Closure of Cavernostomy Sinuses Under Streptomycin Protection. J. D. Murphy and E. R. Koontz.—p. 222.
Diaphragmatic Hernia. H. W. Meyer.—p. 235.
Acute Putrid Abscess of Lung: VI. Late Results of Surgical Treatment. A. S. W. Touroff, R. A. Nabatoff and H. Neuhof.—p. 266.
Transthoracic, Thoracoabdominal Portacaval Anastomosis. V. P. Satinsky, H. P. Redondo Ramirez and L. Gilbert.—p. 272.
Disturbances in Acid-Base Balance During Ether Anesthesia with Special Reference to Changes Occurring During Thoracic Surgery. F. H. Taylor and A. Roos.—p. 289.
Continuous Spinal Anesthesia for Thoracoplasty: Second Report. G. Willauer, J. J. Gartland Jr. and J. J. DeTuerk.—p. 296.
Some Aspects of Cavity Behavior in Pulmonary Tuberculosis. G. A. P. Hurley.—p. 325.

Tumors of the Thymus.—Seybold and co-workers report 45 patients, 28 women and 17 men between the ages of 16 and 68, with thymoma. Tissue was made available for study by surgical removal or by necropsy. Thymoma was defined as a specific tumor of the thymus characterized by the presence of both thymic epithelial and thymocytic cells in varying proportions. The thymoma was associated with myasthenia gravis in 34 patients (75.6 per cent), 22 of whom were aged over 40. Eleven patients (25 per cent) had no evidence of myasthenia gravis at the time they were operated on and subsequently had no symptoms of this disease. Patients with myasthenia gravis or suspected of having it should be examined by roentgenoscopy and by posteroanterior and lateral roentgenography. Characteristically, thymomas occur in the anterior mediastinum in a position anterior to the aortic arch and the base of the heart. Some of the tumors contained calcium in quantities sufficient to be apparent roentgenologically. Peculiar features which would permit a pathological diagnosis on the basis of roentgenologic observations were lacking. Three fourths of the thymomas had a distinct fibrous capsule, while 10 had broken through their capsule to invade adjacent structures and two had spread to pleural surfaces as nodular implants of the tumor. There was no evidence of embolic, lymphogenous or hematogenous metastasis. Surgical treatment was not attempted in four patients because of a poor general condition. Thirty-one of the remaining 41 patients underwent complete removal of the tumor and 10 underwent incomplete removal or biopsy. Myasthenia gravis was the cause of death of three of the five patients who died after operation. There was no evidence of recurrence of the tumor in any of the patients whose tumor was removed completely. The tumor itself was usually fatal in patients with ineradicable lesions. Intensive roentgen therapy for ineradicable tumors seemed to benefit some patients. Exploratory thoracotomy is indicated for all patients with mediastinal tumors whose general condition will permit, because there is no basis clinically or roentgenologically for the accurate pathological diagnosis of these tumors.

Cavernostomy for Residual Cavity.—Murphy and Koontz performed cavernostomy on 23 patients with pulmonary tuberculosis and residual post-thoracoplasty cavities. Cavernostomy was carried out in two stages. Regenerated ribs and muscle bundles overlying the cavity were excised, the parietal pleura exposed and as large an extrapleural space as possible developed in the first stage. Ten to 14 days later, as large an area of the cavity as possible was unroofed by the electrocautery knife or, if the large vessels were threatened, by sharp dissection and a gauze pack placed into the cavity and left there for four days. It was then removed and the sinus packed daily with gauze moistened with an antiseptic solution. After a period varying from three to five months the drainage usually became thin and scanty. The sinus tract narrowed and epithelialized. Closure was attempted if three successive cultures of both the sputum and drainage material were negative and planigrams indicated eradication of the cavity. One gram of streptomycin in two divided doses, 0.5 Gm. each, was administered daily for one week preoperatively and two weeks postoperatively. Sixteen of the 23 patients had the resultant sinus tract closed by a muscle plastic operation, with streptomycin used as an adjunct. Closure was accomplished in 13 of these, who were followed for periods varying from one to two years. They had a negative sputum. Seven patients still have a draining sinus. Three of these were recent cases, in which closure will ultimately be effected. The remaining three were poorly selected cases in which closure could not be accomplished. The residual cavity was definitely eradicated, as revealed by planigraphic studies in 12 of the 16 patients whose sinuses were closed. Three of the remainder had planigraphic roentgenograms consistent with bronchiectasis in the former cavitary area. Two of these had a consistently negative sputum nearly two years after closure. One definite recurrence of sinus and cavity required lobectomy. Cavernostomy with streptomycin as an adjunct offers a satisfactory form of treatment for patients with residual cavities who are not suitable risks for resection.

Maine Medical Association Journal, Portland

41:309-356 (Aug.) 1950

Dicumarol Treatment of Myocardial Infarction, Threatened or Actual. R. S. Martin and E. H. Drake.—p. 310.
Improvement in Care of Newborn, Résumé. A. A. S. Whittier.—p. 313.
Ectopic Pregnancy. C. E. Dunham.—p. 315.
Cystectomy and Uretero-Intestinal Anastomosis for Cancer of Bladder. D. F. Marshall and L. A. Asali.—p. 318.
Transthoracic Nephrectomy for Metastatic Osteogenic Sarcoma of Kidney. D. F. Marshall and E. H. Drake.—p. 320.
Bronchiogenic Carcinoma: Present Concepts as to Diagnosis and Treatment. E. H. Drake.—p. 323.
Rupture of Musculotendinous Cuff of Shoulder. E. G. Asherman.—p. 327.
Use of Prefrontal Lobotomy in Treating Intractable Pain with Review of Literature. E. W. Skwarok and G. L. Maltby.—p. 329.
*Familial Polyposis of Colon. F. B. Clark and J. M. Parker.—p. 331.
The 1949 Poliomyelitis Epidemic. E. M. Cook Jr., T. Anton and E. S. Sherwood.—p. 337.

Familial Polyposis of Colon.—Clark and Parker report the occurrence of polyposis of colon in one family. The mother died of cancer of the colon at 41 years of age. No history concerning her siblings or parents was obtainable. She gave birth to 10 children, three having polyposis of the colon and one having died from cancer of the colon at 34 years of age. The three children of the latter, aged 17, 16 and 14, had polyposis of the colon. It is a disease characterized by a high incidence of malignant degeneration at an early age. The diagnosis is best established on the basis of a familial history and repeated, painstaking examination of the large bowel. The treatment is surgical extirpation of the entire large bowel. In adults treatment should be based on the presumption that malignant degeneration is imminent, making total colectomy necessary. Terminal ileostomy and removal of the colon to the lower sigmoid in one stage may often be feasible in a young patient who is a good operative risk. This may be followed by an abdominal perineal resection of the rectosigmoid. In rare instances where there is no disease in the rectosigmoid, preservation of this segment and anastomosis with the terminal ileum is practicable. The authors believe that, when the disease is sufficiently limited to the rectosigmoid, ileosigmoidostomy or ileoproctoscopy followed by fulguration of the polyps in the remaining rectosigmoid is not rational treatment. Polyps recur rapidly in areas that have been previously fulgurated and are frequently so numerous that fulguration is not practical. Malignant degeneration may occur and advance rapidly. The treatment of this disease in adolescence is fraught with hazards of nutritional deficiencies incident to an ileostomy. It may be possible to predict the age at which malignant degeneration will occur within wide limits on the basis of duration of the disease, the observed size and number of the polyps and the age at which malignant degeneration has occurred in antecedents or siblings. Careful observation and postponement of surgical treatment is justifiable if these factors indicate that malignant degeneration will not occur until after maturity.

Minnesota Medicine, St. Paul

33:753-856 (Aug.) 1950

Better Rural Transfusion Program. A. H. Borgerson.—p. 773.
Psychological Medicine in General Medicine Setting. R. M. Magraw.—p. 776.
The 1949 Cancer Statistical Study: Minnesota Department of Health. N. O. Pearce and D. S. Fleming.—p. 782.
*Infant Methemoglobinemia in Minnesota Due to Nitrates in Well Water. A. B. Rosenfield and R. Huston.—p. 787.
Pituitary Adrenocorticotropic Hormone (ACTH) in Asthma. J. S. Blumenthal.—p. 797.
Renal Tumors. H. Fisketti.—p. 799.

Methemoglobinemia Due to Nitrates.—According to Rosenfield and Huston, methemoglobinemia due to nitrates in well water is widespread in certain rural regions of the United States and Canada. In Minnesota 146 cases of methemoglobinemia from this cause, including 14 deaths, have been reported. Dry and evaporated milk formulas as well as diluted cow's milk formulas, which require large amounts of water as diluent, are most dangerous for infants. Since no infants who were breast-fed developed methemoglobinemia, this seems to be another argument in favor of breast feeding, especially in rural areas. Data are presented on water supplies suspected of being implicated in cases of infant methemoglobinemia in Minnesota. In all but two of these cases, the nitrate nitrogen content of the water was in excess of 20 parts per million. Periodic sampling over a one year period indicated that the nitrate concentration of a well remains fairly constant. Reconstruction of two wells failed to show, as some workers thought, that good well construction for a depth of 10 feet would exclude nitrates. Nitrates seem to occur more frequently in shallow wells (75 feet or less), than in deep wells. No method was found by which nitrates could be removed from water. None of the cases of methemoglobinemia in Minnesota occurred from the use of water containing less than 30 parts per million of nitrate nitrogen (NO_3N). However, 10 parts per million has been accepted as the point above which the water should be viewed with suspicion, because of the possibility of a dangerous level being reached through other factors such as boiling.

New England Journal of Medicine, Boston

243:205-240 (Aug. 10) 1950

Family Studies in Preventive Pediatrics. J. C. Spence.—p. 205.
Psychiatric Factors in Essential Hypertension: II. Follow-Up Study of 74 Cases. W. I. Tucker.—p. 211.
Intestinal Lipodystrophy (Whipple's Disease): Report of Case. W. S. Revelo.—p. 216.
Liquor Adulterated with Lye as Cause of Dysphagia and Stricture of Esophagus. U. K. Kiviranta.—p. 220.
Vitamin B12 and Pernicious Anemia (Concluded). M. B. Strauss.—p. 222.

243:241-280 (Aug. 17) 1950

Anomalies of Gastrointestinal Tract: Review of Literature and Report of Two Unusual Cases. R. B. Miller and A. O. Hampton.—p. 241.
*Therapeutic Experiences with Subacute Bacterial Endocarditis with Special Reference to Failures. D. Littmann and R. S. Schaaf.—p. 248.
*Febrile Thrombopenic Purpura with Hemolytic Anemia and Platelet Thrombosis. P. T. Goldenberg, J. E. Thayer and L. P. Hastings.—p. 252.
Hypertension. D. Loofbourow and R. S. Palmer.—p. 257.

Subacute Bacterial Endocarditis.—Littmann and Schaaf compare therapeutic experiences in subacute bacterial endocarditis from 1947 to 1949 with those for the preceding three years. The adequately treated failures, numbering 23 cases, were separately compared with the 52 recoveries. Early recog-

nition and adequate antibiotic therapy were important in obtaining cures and limiting permanent structural damage. Most deaths (17 of 23) occurred as a consequence of irreversible cardiac, renal or cerebral changes, despite sterilization of the blood stream. Infection was present terminally in only six cases, and four of these were considered to be due to truly resistant organisms. The nutritional state of the patients was found to be of prognostic value. In approximately half the failures the patients were poorly nourished, and only 6 per cent of the cured patients were so designated. Uremia and congestive failure were ominous events during the course of subacute bacterial endocarditis and commonly foreshadowed an unsuccessful termination. Patients with the most serious heart disease fared the least well. There was a relatively high incidence of congenitally bicuspid aortic valves in those who died. Although more resistant to therapy, subacute bacterial endocarditis was found to be less frequent (by almost 50 per cent) in recent than in former years. The reduction in total numbers was thought to be due in part to the currently widespread and probably justified use of antibiotics in patients with valvular heart disease for diagnoses other than bacterial endocarditis.

Thrombopenic Purpura.—A clinical syndrome characterized by fever, a rapidly progressing anemia, mild icterus, thrombopenia, central nervous system manifestations and death in a relatively short time was first described by Moschcowitz in 1925. Since that time a limited number of cases that seemed to fit this picture clinically and pathologically have appeared in the literature. The outstanding features at necropsy were numerous petechial hemorrhages of the heart, kidneys, liver and brain, which microscopic examination revealed to be due to platelet thrombi. As yet, this peculiar sequence of events has not been explained, but in all likelihood it is initiated by a spontaneous deposition of the blood platelets, owing either to an upset in the coagulating mechanism of the blood or to a preceding capillary and arteriolar injury. The authors describe the case of a young woman, aged 23, who had this type of disorder and in whom psychiatric manifestations were so prominent that she was at first believed to have a major psychosis and was placed in a mental institution. No effective treatment has so far been found for this disease.

New Orleans Medical and Surgical Journal

103:51-100 (Aug.) 1950

Assurance as to Advantages and Safety of Radioactive Iodine Treatment of Hyperthyroidism. S. Hertz.—p. 51.
Myocarditis. M. D. Hargrove, W. M. Hall, W. M. Allums and T. H. Gandy.—p. 63.
Malingering. N. J. Bender.—p. 71.
Prevention of Deafness. E. G. Walls.—p. 74.
*Streptomycin Therapy for Childhood Tularemia. H. B. Levy, C. H. Webb and J. D. Wilkinson.—p. 78.
Studies of Diets of Pregnant Women in Mississippi: II. Diet Patterns. J. H. Ferguson and A. G. Keaton.—p. 81.
Notes on Medical History of the Panama Canal. R. E. Mitchell Jr. —p. 87.

Streptomycin for Childhood Tularemia.—According to Levy and his associates, 48 children with tularemia were treated at the Charity Hospital of Shreveport, La., during the period May 1943 through July 1949. Twenty-four children were treated with streptomycin. The average total dose administered to a patient was 8.37 Gm., given for an average duration of 7.46 days; later dosage averaged 1 Gm. daily for five to six days (125 mg. at three hour intervals). This is in excess of the dose recommended by Foshay, who suggests 0.5 Gm. daily for two days followed by 0.25 Gm. daily for four days or, as an alternative course, 0.5 Gm. daily for six days. There were no instances of toxicity or sensitivity, despite the relatively large doses used at first; with the lower dose and shorter course now advocated, this danger will be lessened even more. The rapid response to streptomycin observed in every child in this series proves the efficacy of this antibiotic against Pasteurella tularense. Since the diagnosis of tularemia in childhood may be extremely difficult, especially in those cases in which an adequate history is lacking, there is justification for inclusion of a therapeutic trial with streptomycin for every severely ill child who fails to respond to other treatment.

New York State Journal of Medicine, New York

50:1871-1982 (Aug. 15) 1950

Treatment of Acne Vulgaris. H. H. Bauckus.—p. 1917.
*Seborrheic Dermatitis: Supplemental Treatment with Vitamin B12. G. C. Andrews, C. F. Post and A. N. Domonkos.—p. 1921.
Impact of Psychiatry on Therapy in Dermatology. H. Sharlit.—p. 1926.
Further Experiments on Prolonging Local Anesthesia with Insoluble Anesthetic Bases. S. Monash and A. Guiducci.—p. 1929.
Control of Tinea Capitis. A. C. Cipollaro and A. Brodey.—p. 1931.
N-Ethyl-O-Crotono-Toluide (Eurax) as Antipruritic. S. M. Peck and T. J. Michelfelder.—p. 1934.
Treatment of Localized (Pretibial) Myxedema with Hyaluronidase. D. Rosman.—p. 1939.
Failure of Undecylenic Acid to Cure Psoriasis. S. C. Atkinson Jr. and G. M. Lewis.—p. 1943.
Pneumoperitoneum Versus Pneumothorax. J. S. Edlin and S. Bassin. —p. 1947.
Chronic Biliary Disease in General Practice. J. A. Porcello.—p. 1956.
Treatment of Backaches by Infiltration of Anesthetic Oils. P. Lahvis. —p. 1959.
Application of Epithelial Grafts to Oral and Other Facial Cavities. J. E. Sheehan and W. A. Swanker.—p. 1963.

Vitamin B_{12} in Seborrheic Dermatitis.—Andrews and his associates used vitamin B_{12} in treatment of 101 patients with dermatological disorders. They were prompted to use this preparation because of the beneficial effects obtained with crude liver extract and vitamin B complex in metabolic and nutritional deficiency states. While many patients with seborrheic dermatitis have a mild, usually normocytic or hypochromic anemia, the response of the skin disease could not be judged from the red blood cell count, hemoglobin, hematocrit studies or reticulocyte count. The vitamin was administered by intramuscular injection. Local treatment was not neglected. Patients with secondary infections of the seborrheic areas were treated with sulfonamides and penicillin. Improvement usually manifests itself after two or three injections. Many of these patients have no recurrences. A mild recurrence usually can be treated satisfactorily with a few additional vitamin B_{12} injections, and recurrences have been prevented entirely by a maintenance dose of 15 or 30 micrograms of the vitamin given intramuscularly every two or three weeks. Where other metabolic, endocrine and nutritional factors are implicated and appropriately treated, recurrences will not appear. Of 37 patients with seborrheic dermatitis who were studied thoroughly, 16 were cured, 16 improved, 3 only slightly improved and 2 were worse. The authors conclude that these results are superior to those that can be obtained by local treatment alone. They believe that this is essentially a nutritional disease. Pityrosporum ovale, other cryptococci, staphylococci and streptococci are probably saprophytes or secondary invaders. They account for many of the inflammatory features of the disease.

Northwest Medicine, Seattle

49:499-566 (Aug.) 1950

Sterility. R. J. Crossen.—p. 521.
Lower Nephron Nephrosis. R. L. Cutter.—p. 526.
Esophageal Electrocardiogram. R. F. Foster and R. H. Thayer.—p. 530.

49:567-650 (Sept.) 1950

Nerve Blocks as Aid in Diagnosis and Therapy of Disease. J. J. Bonica. —p. 593.
Neurologic Syndrome About Face and Head. J. T. Robson.—p. 596.
Dr. D. S. Maynard, Pioneer Physician of Seattle. M. W. Prosch. —p. 593.
Some Current Medical Aspects of Thyroid Disease. M. J. Goodman. —p. 600.
Some Surgical Aspects of Thyroid Disease. J. M. Guiss.—p. 602.
Tumors of Thyroid Gland. W. L. Lehman.—p. 604.

Oklahoma State Medical Assn. Jour., Oklahoma City

43:351-396 (Aug.) 1950

Oklahoma's Future Role in Cancer Program of United States. S. Binkley. —p. 353.
Developments in Treatment of Macrocytic Hyperchromic Anemias: Report of Case of Pernicious Anemia with Sub-Acute Combined Degeneration Treated with Vitamin B12. V. Sundgren.—p. 356.
Medical and Hospital Insurance Is the Answer. J. P. Cox.—p. 358.
Effectiveness of Methylcellulose in Gastrointestinal Disturbances. V. H. Musick.—p. 360.
Practical Precautions During Labor. B. D. Faris.—p. 365.

43:397-440 (Sept.) 1950

The Crippled Lung. J. W. Gale.—p. 400.
Indications for and Results of Keratoplasty. C. A. Royer.—p. 405.
Differential Diagnosis of Red Eye. A. N. Lemoine Jr.—p. 407.
Goniotomy in Congenital Glaucoma. E. N. Robertson.—p. 409.

Pennsylvania Medical Journal, Harrisburg

53:785-928 (Aug.) 1950

Appraisal of Some Analgesic Agents and Methods. E. M. Papper. —p. 801.
Reconstruction of Common Bile Duct. I. S. Ravdin.—p. 807.
Recent Advances in Surgical Treatment of Carcinoma of Esophagus: Discussion of Cervical Esophagogastrostomy. F. F. Allbritten Jr. and J. H. Gibbon Jr.—p. 811.
Toxemias of Pregnancy. J. J. Kocyan.—p. 817.

Plastic and Reconstructive Surgery, Baltimore

6:1-96 (July) 1950. **Partial Index**

Surgical Treatment of Bifid Nose. J. P. Webster and E. G. Deming. —p. 1.
One Stage Surgical Repair of Gastrochisis (Omphalocele) by Cutis Graft Technic. J. E. Kearns and B. G. Clarke.—p. 41.
Layer Resection of Cavernous Hemangioma of Face Followed by Plastic Restoration. M. González Ulloa.—p. 46.
Total Pharyngoneoplasty. R. Farina.—p. 58.
Medial Cleft of Lower Lip and Mandible: Case Report. A. D. Davis. —p. 62.
Lateral Facial Clefts. H. M. Blackfield and N. J. Wilde.—p. 68.

Public Health Reports, Washington, D. C.

65:1039-1074 (Aug. 18) 1950

Bactericidal Efficiency of Quarternary Ammonium Compounds. C. T. Butterfield, E. Wattie and C. W. Chambers.—p. 1093.
Haplomycosis in Montana Rabbits, Rodents, and Carnivores. W .L. Jellison.—p. 1057.

65:1075-1110 (Aug. 25) 1950

Two Surveys of Methods Used by Public Health Laboratories for Examination of Stool Specimens for Salmonellae, Shigellae, and Protozoa. O. Felsenfeld.—p. 1075.
Role of Morbidity Reporting and Case Registers in Cancer Control. S. J. Cutler.—p. 1084.

65:1111-1146 (Sept. 1) 1950

Studies of Pulmonary Findings and Antigen Sensitivity Among Student Nurses: VI. Geographic Differences in Sensitivity to Tuberculin as Evidence of Nonspecific Allergy. C. E. Palmer, S. H. Ferebee and O. S. Petersen.—p. 1111.
*Geographic Distribution of Pulmonary Calcification Among University Students in Ohio. J. A. Prior, J. W. Wilce and W. Palchanis. —p. 1132.

Pulmonary Calcification in Students.—This study by Prior and his associates is based on the records of 4,829 students who entered Ohio State University in the fall of 1946 and 1948. Preliminary histoplasmin and tuberculin skin tests were required, and a satisfactory roentgenogram of the chest taken at the time of admission had to be available. The group was further limited to lifetime residents of a given county. The distribution of cases of pulmonary calcification in Ohio followed a definite geographic pattern, which closely parallels the geographic distribution of histoplasmin reactors but does not correspond to the distribution of tuberculin reactors. The incidence of tuberculin reactors tends to be higher in the metropolitan areas and lower in rural sections. The incidence of both pulmonary calcification and histoplasmin reactors tends to be higher in the rural sections than in urban areas and also shows a definite geographic pattern. Although many cases of calcification are undoubtedly due to tuberculosis, these facts indicate that most pulmonary calcification in Ohio and other Middle Western States is probably the result of a benign, widespread form of histoplasmosis or an antigenically related agent or agents.

65:1147-1174 (Sept. 8) 1950

*Relapse Following Apparent Arrest of Leprosy by Sulfone Therapy. P. T. Erickson.—p. 1147.

65:1175-1201 (Sept. 15) 1950

Availability of Fluorine in Sodium Fluoride vs. Sodium Fluosilicate. F. J. McClure.—p. 1175.
Use of Chick Embryo for Isolation of Brucella: Multiplication of Organism in Yolk Sac and Selection of Embryo Age Optimal for Isolation from Blood. K. Gay and S. R. Damon.—p. 1187.

Relapse After Sulfone Therapy in Leprosy.—Erickson reports the recent discovery at Carville of the reactivation of leprosy in six patients in whom it was supposedly arrested by sulfone treatment. Three of these cases, in which there was reappearance of leprosy bacilli in the skin without other manifestations, were classed as subclinical relapses. In the remainder, there were, in addition, unquestionable leprous skin lesions or a true clinical relapse. The disease was arrested by sulfone drugs in 77 patients who had active disease when treatment was begun. Only 33 of these patients were kept under observation with routine clinical and laboratory examinations. All had the lepromatous type of leprosy. The duration of follow-up varied from six months to five years. Among the 33 patients followed, 22 received glucosulfone sodium or sulfoxone sodium in smaller doses, either continuously or interruptedly after arrest of the disease. Eleven patients received no antileprotic remedy after the disease became inactive. Six relapses occurred among the 33 patients. True clinical relapses, of which there were three, occurred only in the group that received no treatment after arrest of the disease. These relapses occurred two to three years after the arrest. Subclinical relapses occurred in both groups; two in the group not treated after arrest and one in the group treated. The latter patient, however, had received a relatively small amount of sulfoxone sodium before the lesion became arrested. The incidence of relapse seems to be lower if sulfone treatments are continued after inactivation of the leprosy.

Rhode Island Medical Journal, Providence

33:333-388 (July) 1950

Diverticulitis and Cancer of Colon. J. J. Morton.—p. 347.
Industrial Medicine and the Private Practitioner. J. J. Poutas.—p. 350.
Problems of General Practice and Their Solutions. C. E. Millard. —p. 354.

Southern Surgeon, Atlanta, Ga.

16:729-836 (Aug.) 1950

*Treatment of Tuberculous Psoas Abscess. M. J. Hoover Jr.—p. 729.
Postoperative Adhesions: Case Report. W. L. Peple Jr.—p. 737.
Satisfactory Method for Dressing Severe Contusion Lacerated Abrasion Wounds of Face. P. N. Pastore.—p. 744.
Streptomycin in Treatment of Granuloma Inguinale of Cervix Uteri and Vulva. R. H. Hoge and A. M. Salzberg.—p. 746.
Some Electrolyte Considerations in Field of Surgery. R. A. Neubauer, R. R. Porter and R. W. Frelick.—p. 754.
Pulmonary Blebs and Bullae. G. A. Welchons and J. R. Massie Jr. —p. 768.
Multiple Metastasizing Carcinoids of Ileum with Simultaneous Papillary Adenomas of Colon Complicated by Intussusception and Gangrene: Case Report with Operation and Recovery. C. L. Coleman and M. Markowitz.—p. 777.
Osteoma of Cranial Vault and Base: Three Cases Illustrating Two Varieties. J. M. Meredith.—p. 785.
Ewing's Tumor of Vertebrae. E. K. Carter and J. W. Compton.—p. 796.
Hemangioendothelioma: Review of Literature with Report of Two Cases. Q. J. Legg and W. M. Fitch.—p. 803.
Comparative Study of Effects of Parasympathetico-Mimetic Drugs on Urinary Bladder. A. I. Dodson and D. R. Gilbert.—p. 812.
Surgical Management of Ureteropelvic Obstruction. A. I. Dodson and D. Gilbert.—p. 816.

Treatment of Tuberculous Psoas Abscess.—According to Hoover, the tuberculous abscess is one of the serious complications of tuberculosis of the spine. This article concerns the treatment of the psoas abscess, which results from the burrowing of the detritus along the fascia of the iliopsoas muscle. Because of its superficial manifestation, this abscess often requires differentiation from the various retroperitoneal abscesses and the iliac fossae abscesses of pyogenic origin. Another problem arising from the tendency of the psoas abscess to become superficial is pressure necrosis of the skin, which may lead to a spontaneous rupture and mixed infection. Aspiration of the abscess with a small needle was the method of choice before the introduction of streptomycin. Surgical incision was feared because of the danger of a mixed infection and of the resultant draining sinus tract. Psoas abscesses usually point in Petit's triangle, in the groin or in the thigh region. The incision should be made with strict aseptic technic in a sound area of skin a suitable distance from the "pointing spot." The contents are removed; the cavity is flushed with isotonic sodium chloride solution, and streptomycin solution is instilled. Streptomycin may also be given intramuscularly, but when this is done, sufficient levels may not be reached in the abscess cavity because of the poor blood supply of the tuberculous tissue. The author describes several methods of surgical drainage and local use of streptomycin in the psoas cavity. The instillation of streptomycin solution into the cavity, followed by closure in layers of the incision, was the method used at Johns Hopkins Hospital. The immediate results were dramatic when surgical drainage was used in conjunction with streptomycin applied locally.

FOREIGN

An asterisk (*) before a title indicates that the article is abstracted. Single case reports and trials of new drugs are usually omitted.

British Journal of Ophthalmology, London

34:457-516 (Aug.) 1950

The Water-Drinking Test. W. Leydhecker.—p. 457.
Permeability of Blood-Aqueous Barrier to Fluorescein During Water-Drinking Test in Glaucomatous Eyes. W. Leydhecker.—p. 480.
Arcuate Lens Opacities of Mongolism and Cataracts of Similar Appearance. R. F. Lowe.—p. 484.
Trabeculs in Chronic Simple Glaucoma, with Special Reference to Gonioscopic Appearance of Blood in Canal of Schlemm. H. E. Hobbs.—p. 489.
Significance of Conjunctival Aneurysms in Diabetics. C. McCulloch and T. J. Pashby.—p. 495.
Intra-Ocular Involvement in Case of Xanthomatous Biliary Cirrhosis. N. Lewis.—p. 506.
Case of Watering Eye Due to Pterygium. F. J. Damato.—p. 509.
Appliances—Non-Magnetic Foreign-Body Extractor. H. B. Stallard. —p. 511.
Dark Glasses. F. A. Williamson-Noble.—p. 513.

British Medical Journal, London

2:471-534 (Aug. 26) 1950

Methods of Education. J. A. Lauwerys.—p. 471.
Art of Lecturing. G. P. Meredith.—p. 475.
Methods and Men in the Teaching of Clinical Medicine. H. Cohen. —p. 478.
Training of Clinical Teachers. R. D. Lawrence.—p. 481.
Clinical Evaluation of Effects of Drugs on Medical Students as a Teaching Method. A. Wilson, G. S. Crockett, A. N. Exton-Smith and H. Steinberg.—p. 484.
Mechanical Aids to Instruction. R. Ollerenshaw.—p. 488.
A G.P. on His Clinical Training. D. M. Johnson.—p. 493.
Some Comments on Medical Education in Great Britain by a London Medical Student.—p. 496.

2:535-560 (Sept. 2) 1950

Effects of Hypervitaminosis A on Foetal Mouse Bones Cultivated in Vitro. H. B. Fell and E. Mellanby.—p. 535.
*Respiratory Studies in Paralytic Poliomyelitis. R. B. Bourdillon, E. Davies-Jones, F. D. Stott and L. M. Taylor.—p. 539.
Poisoning by Organic Phosphorus Insecticides. P. L. Bidstrup.—p. 548.
Food Poisoning in Sheffield in 1949. E. L. Millar and M. Pownall. —p. 551.
Thrombocytopenic Purpura Due to Quinidine. G. Moodie.—p. 553.
Ollier's Disease: Dyschondroplasia. S. G. Nardell.—p. 555.
Lysivane Therapy for Parkinsonism. H. Palmer and D. J. A. Gallagher. —p. 558.
Relative Incidence of Gastric and Duodenal Ulcers. E. M. Brooke. —p. 560.

Respiratory Studies in Paralytic Poliomyelitis.—The observations reported by Bourdillon and his associates were made during the 1949 epidemic of poliomyelitis. Numerous measurements of tidal air were made with a spirometer on patients and on healthy subjects in Both and Drinker respirators and on patients after respirator treatment for poliomyelitis. Among the subjects studied were nine patients for whom respirator treatment was considered essential. Five of these were too ill for experimental tests and died without having had any measurements of tidal air. The authors give data on the four surviving respirator patients and of the healthy subjects. The measurements showed a wide range of variation from day to day in most cases. The authors believe that in the treatment of poliomyelitis with respiratory involvement there is need for measurements of vital capacity and tidal air, unless frequent measurement of blood oxygen and carbon dioxide are practicable. Early measurements of vital capacity are suggested in order to detect the first signs of respiratory involvement, with a view to resting the muscles concerned by prompt use of a respirator. The tidal air measurements are indicated as a rough guide to the correct setting of respirator pressures, to avoid underventilation or overventilation. The potential dangers of hyperventilation are discussed, and measurements are given showing the ease with which they are obtained in respirators. The authors describe tests on the use of the prone position in respirators and stress the importance of using this position, especially in bulbar cases. They suggest improvements in the Both respirator, such as provision for slower speeds and reduction in the angle of slope and in the thickness of the front panel.

Edinburgh Medical Journal

67:225-260 (June) 1950

Acid Secretion of the Stomach. C. F. W. Illingworth.—p. 225.
Large Gastric Ulcer. A. W. Branwood.—p. 234.
Obesity. A. P. Meiklejohn.—p. 243.
Case of Fat Embolism in Early Childhood. H. G. Howell Richards. —p. 252.
Bronchial Cancer as a Cause of Heart Block. C. K. Robertson and J. T. R. Rusell.—p. 257.

Journal of Clinical Pathology, London

3:191-300 (Aug.) 1950. Partial Index

Meningeal Tumours: Review. D. S. Russell.—p. 191.
Giant Cell Granuloma Associated with Lesions Resembling Polyarteritis Nodosa. G. H. Howells and I. Friedmann.—p. 220.
Bone Marrow in Hutchinson's Syndrome. A. Piney, J. Mallarmé and M. S. Ross.—p. 230.
*Complement Fixation Test for Herpes Simplex Infections. J. A. Dudgeon.—p. 239.
Fractionation of Serum Proteins Using Sodium Sulphate. N. H. Martin, R. Morris and M. Smith.—p. 266.
Renal Threshold for Bilirubin. H. E. Vickers.—p. 271.
Nature of Tissue Fluid in Oedema of Toxaemia of Pregnancy. C. L. Mukherjee and A. D. T. Govan.—p. 274.

Complement Fixation Test for Herpes Simplex.—According to Dudgeon the serologic diagnosis of virus infections depends for the most part on neutralization and complement fixation tests. Both have been described in herpes simplex infections. The neutralization test is used almost exclusively at present, owing to the conflicting results obtained by the complement fixation. The author attempted to prepare a more satisfactory antigen from the developing chick embryo, as was done with other viruses. He reports on a preparation of a chorioallantoic membrane antigen and its use in the diagnosis of herpes simplex infections. Antigens prepared from the chick embryo have several advantages over antigens prepared from animal and, in particular, brain tissue. They are easy to prepare, they have a high virus content and are bacteriologically sterile and the risk of nonspecific results is reduced. At the same time control antigens from uninfected tissue are easily prepared. The chorioallantoic membrane was used in one case as the source of antigen in preference to the amniotic and allantoic fluids, which, although they showed positive fixation, were seldom as constant in titer and on occasions were anticomplementary. The interpretation of any complement fixation reaction depends to a great extent on the specificity of the reaction. The more sensitive and the more specific the test can be made, the greater is its value. This quality of specificity is largely dependent on the antigen itself. In the present investigation nonspecific results were almost entirely eliminated by (1) the use of the chorioallantoic membrane antigen, (2) the preparation of hyperimmune serums with homologous tissue and (3) inactivation of the serums at 62 C. for 15 minutes. The test appeared to be of value as an alternative diagnostic method in herpes simplex infections, in particular when a large number of serums have to be examined. It may also be useful in following the course of antibody production in cases of recurrent herpes infections.

Journal of Laryngology and Otology, London

64:375-454 (July) 1950

Clinical Detection of Auditory Recruitment. P. Denes and R. F. Naunton.—p. 375.
*Rubella Congenital Inner-Ear Deafness. B. Hiller.—p. 399.
Studies on Sensory Epithelium of Labyrinthine Crista Ampullaris in Fishes. T. Vilstrup.—p. 420.

Rubella Congenital Inner Ear Deafness.—Hiller reviews the results of examination of 42 children with congenital inner ear deafness, the mothers of some of whom had had rubella during the Australian rubella epidemics of 1937-1940. The children have now reached the age at which they are able to offer full cooperation for examination of their hearing.

The deafness in 32 cases was due to rubella occurring in the mother in the early months of pregnancy; the other 10 are classed as nonrubella inner ear deafness cases. The degrees of deafness and the types of audiometric curves of various groups of children were analyzed. The average degree of deafness in the rubella-deaf group is less than that in the nonrubella cases. The audiograms of the rubella-deaf subjects show a great diversity of patterns. In general, low tones are less affected than high tones, but any downward trend in the curve of the audiogram is less steep than in typical inner ear deafness. The incidence and severity of rubella deafness and also the incidence of accompanying rubella retinitis appear to be directly dependent on the severity of the maternal rubella infection. Analysis of supposed nonrubella deafness made the authors believe that some of these cases may have resulted from maternal infection with rubella during early pregnancy. They also suggest that cases of congenital inner ear deafness with typical audiometric curves are probably hereditary in origin, while those with atypical graphs may be the result of antenatal infection, such as rubella, in the mother.

Journal of Tropical Medicine and Hygiene, London

53:167-192 (Aug.) 1950

Attempts to Cultivate Rabies in Cell-Free Medium. R. Kirk, M. A. Haseeb and A. T. Davis.—p. 167.
*Ascorbic-Acid (Vitamin-C) Deficiency in the Tropics. E. Stransky, D. F. Dauis-Lawas and C. Vincente.—p. 170.
Experiment in Hydrocyanic Acid Gas Fumigation as Control Measure Against Plague. J. I. Roberts.—p. 175.

Vitamin C Deficiency in the Tropics.—According to Stransky and his associates nutritional problems are becoming more important in the tropics because millions of persons are going to the cities and are shifting from agriculture to mining, industry, commerce and clerical work. People living in large centers of population in the tropics have no means for preservation of food; hence a diet consisting mostly of nonperishable foods must be adopted. While in rural districts there is frequently plenty of fresh food, such as fruit and vegetables, the city dwellers live mostly on carbohydrate-rich food. Infants are exclusively breast fed or are given only diluted condensed milk, since condensed milk can be kept without refrigeration. Fresh vegetables and fruits are not given to infants, even in the second year of life. The authors determined the vitamin C (ascorbic acid) content in 20 samples of human milk, in the blood plasma of 89 nursing mothers and in the blood plasma of 124 children, 32 of them infants below the age of 1 year. Ninety per cent of all examined samples revealed levels below normal and 60 per cent far below normal, while 30 per cent showed levels suggestive of scurvy. The authors conclude that ascorbic acid deficiency is a public health problem of paramount importance in the tropics.

Lancet, London

2:313-352 (Aug. 26) 1950

Discussion Methods in Preclinical Teaching. M. L. Johnson.—p. 313.
Education for General Practice: Psychosocial Factors. H. V. Dicks.—p. 317.
Origins and Outcomes of Patient's Stay in Hospital: Report on Project of Teaching Social Medicine. E. Addiscott, J. H. F. Brotherston and R. C. MacKeith.—p. 320.
Teaching of Social Medicine in University of Sheffield. W. Hobson and J. Pemberton.—p. 323.
"An Unconscionable Time A-Dying": Some Outmoded Practices Still Current. W. P. U. Jackson.—p. 324.

Medical Press, London

224:195-214 (Aug. 30) 1950. **Partial Index**

Indications for and Prognosis in Surgical Treatment of Gastric and Duodenal Ulcers. W. R. S. Hutchinson.—p. 203.
*Modern Trends in Spinal Anaesthesia. A. R. Hunter.—p. 206.

Modern Trends in Spinal Anesthesia.—Hunter feels that it is now possible to make a much truer assessment of spinal anesthesia. He reviews the physical factors, the physiological and circulatory factors, the neurophysiological aspects and the nervous complications. Limits to the use of spinal anesthesia are set by the competence of the anesthetist, the physical state of the patient and the type of operation to be performed. In the hands of the inexperienced, both inadvertent overdosage and partial failure will be common. When the method is used by the unintelligent, who believe that the dose is "the contents of one ampule," frequent catastrophes are inevitable. Contraindications to spinal anesthesia are local or general sepsis and disease of the spinal cord. The most serious contraindication is cardiovascular insufficiency of such a degree that the patient is unable to compensate for the vasodilatation which is produced. Patients with serious blood volume deficiency come into this group, even if the blood pressure is maintained at normal levels by compensatory vasoconstriction. So also do those with severe myocardial failure. The patient's temperament is not a guide to his suitability for spinal anesthesia. With adequate premedication the most nervous patient can be given a spinal anesthetic. Spinal anesthesia is unsuitable for operations above the xiphisternum, nor is it likely to give satisfactory results when used alone for operations in the upper part of the abdomen, since in this region the segmental level of the autonomic innervation of the viscera is so high that complete vasomotor paralysis is an almost inevitable accompaniment of adequate spinal block. For operations on the colon, on the small bowel, for suprapubic exploration of the bladder and for all operations deep in the pelvis, spinal anesthesia provides an unvarying degree of relaxation and an immobility of the viscera that is not obtainable with any other anesthetic technic.

South African Journal of Clinical Science, Cape Town

1:73-148 (June) 1950

Acute Intestinal Obstruction with Special Reference to Closed Loop and Strangulating Lesions in the Bantu: Clinical Study. J. Hamman and D. Alldis.—p. 73.
Syndrome of Malignant Malnutrition: Observations on Relation of Serum Proteins to Occurrence of Oedema and Effect of Diet. E. Janssen and J. S. le Roux.—p. 100.
*Gravitational Leg Syndromes. W. Girdwood.—p. 114.

Gravitational Leg Syndromes.—Girdwood points out that, although much discomfort, ill health and restriction of normal activities are caused by chronic varicose ulcers, varicose veins and postphlebitic lesions, little permanent success has resulted from the treatment usually employed. The temporary nature of the relief afforded has been due to the failure to appreciate the magnitude of the problem involved. Gravitational leg syndromes are an assortment of disorders in which a series of vicious cycles occur, constantly aggravating the condition and leading to a final picture involving venous antigravity failure, failure of the "pump" and a chronic, indurated leg ulcer with scarring. Three links should receive attention in the cycles which predominate: the ulcer, the pump and the veins. In the strip grafting which the author recommends the indurated scarred tissue about the ulcer and the ulcer itself are excised. It is important to preserve a healthy layer of covering to the tendons, which is usually possible. A long incision is made extending above the ulcer to the upper part of the leg and often another below the ulcer. The deep fascia is incised in the line of the incision or excised, and the underlying muscle is exposed. If the communicating veins are incompetent, these are divided. If there is foot drop, lengthening is done at this stage at the level of muscular fibers. A split skin graft, usually in one piece, is then applied to this raw area. The three irreversible factors, scar, lymphedema and skin stricture, are overcome by this procedure. The graft, placed on a healthy base, obtains its nutrition from the deep tissues through the muscle; because of the continuity of the graft on muscle with the graft over the previous ulcer site, the nutrition continues to that area and even to the neighboring skin. Skin stricture is relieved by strip grafting as the graft acts as a "let in" procedure, thus overcoming the stricture. The operation results in firm support to the communicating veins and allows the correction of antigravity failure of the communicating veins. Shortening of the Achilles tendon is corrected, and ankle movements are restored. Strip grafting attacks not only the ulcer problem but the vein problem, and by mobilization of the ankle and removal of pain it reconstitutes the pump.

Tubercle, London

31:197-222 (Sept.) 1950

Tuberculosis in Holland. L. H. A. Hoefnagels.—p. 198.
Treatment of Tuberculous Meningitis. C. J. McSweeney.—p. 210.

Acta Tuberculosea Scandinavica, Copenhagen

24:1-176 (No. 1-2) 1950. **Partial Index**

Duration of Fatal Pulmonary Tuberculosis. B. Andersen.—p. 1.
*Tuberculin Sensitivity in Boeck's Sarcoid. R. T. Bjørnstad.—p. 15.
Observations on Biological Properties of BCG Treated by Freeze-Drying. J. Böe and R. I. N. Greaves.—p. 38.
*Tracheobronchial Tuberculosis and Streptomycin. W. Mascher and S.-B. Mattson.—p. 114.

Tuberculin Sensitivity in Boeck's Sarcoid.—Bjørnstad used up to 10 mg. doses of tuberculin in intracutaneous tests of 71 patients with Boeck's sarcoid and with definite skin lesions. Fifty patients (70.4 per cent) had a negative reaction and 21 (29.6 per cent) a positive reaction. Twelve patients had a positive reaction to 0.1 mg.; two had a positive reaction to 0.01 mg., but none had a positive reaction to smaller doses. The tuberculin sensitivity of the tuberculin-positive patients with Boeck's sarcoid is weak. Fifty of the patients were aged over 40; 33 had a negative reaction to tuberculin. Nine of the 50 patients with a negative reaction had been exposed to tuberculosis in their homes. The chest roentgenograms of 11 of these 50 patients showed calcium shadows, which most likely indicated a previous tuberculous infection. The frequency of the negative reactions must be due to Boeck's sarcoid itself and cannot be due to the fact that the patients with a negative reaction have escaped tuberculous infection. It is possible that a large number of patients with sarcoid had a negative reaction to tuberculin because their tuberculous infection had been cured. Negative intracutaneous tests with up to 1 mg. of tuberculin will afford valuable aid in differentiation of Boeck's sarcoid and tuberculosis. The diagnostic significance of negative or weak reactions to tuberculin is greatest in patients with skin lesions or involvement of lymph nodes, while negative reactions are of lesser diagnostic significance in patients with pulmonary involvement resembling miliary tuberculosis. From the etiological point of view the absent or weak tuberculin sensitivity is due to a hitherto unknown chronic infection which causes increased resistance to tuberculosis. The tuberculin anergy and resistance to tuberculosis in Boeck's sarcoid may or may not have a purely tuberculous etiology.

Streptomycin in Tracheobronchial Tuberculosis.—Mascher and Mattson treated 22 patients with tracheobronchial tuberculosis with streptomycin. The drug was administered by aerosol, 0.5 Gm. dissolved in 10 cc. of isotonic solution of sodium chloride daily, and by intramuscular route, 1 Gm. in two divided doses of 0.5 Gm. daily. Five patients were given aerosol treatment alone; nine received the drug by intramuscular route alone; two were treated simultaneously by aerosol and by intramuscular injection, and six were given alternating aerosol and injections. Bronchoscopic examination showed that healing of the local process occurred in 17 patients, five of whom were treated by aerosol alone, eight by injections alone, one by aerosol and injection simultaneously and three alternately by aerosol and by injection. Three patients were improved, and treatment failed in two. Nine patients had become free from Koch's bacilli. Results of bacterial tests were positive in eight patients whose local process was healed, but six of them had active pulmonary lesions which accounted for the presence of bacteria. Relapse occurred in three patients. Three patients had vestibular symptoms, but treatment had to be discontinued in only one. Two patients had allergic symptoms. Desensitization was achieved in one with 0.01 Gm. of streptomycin given twice daily for eight days and doses increased gradually to 0.02, 0.03, 0.05, 0.1 and 0.25 Gm. twice daily. Fibrotic stenosis developed in five. Treatment for four to six weeks with a total dose of 50 to 60 Gm. should be sufficient for mild lesions of mucous membranes; the authors caution against too early discontinuance of treatment, because of threatened relapses. Combined treatment by aerosol and by intramuscular route is recommended because greatest concentration of the drug in the affected tissues, i. e., in the bronchial wall, may thus be achieved. Endobronchial tuberculosis should be treated with streptomycin before collapse therapy is considered.

Chirurg, Heidelberg

21:261-324 (May) 1950. **Partial Index**

Intraoperative Blood Transfusion. J. Rehn.—p. 266.
Determination of Time and Extent of Blood Transfusion to Prevent Surgical Shock. B. Löhr.—p. 270.
Structure and Mechanism of Aortic Wall with Consideration of Surgical Treatment in Stenosis of Isthmus. A. Benninghoff.—p. 276.
Modification of Trachea by Goiter and Significance of Preoperative Roentgen Examination in Thyroidectomy. F. W. Wichmann and P. Schmidt.—p. 280.
Unsolved Problems in Vascular Surgery. H. Gesenius.—p. 284.
Preoperative Irradiation in Cancer of Breast: Pathologic Studies. E. Stenger.—p. 292.
Technic of Extirpation of the Larynx. H. Hellner.—p. 297.
*Should the Right Ventricle Be Punctured During Venous Air Embolism? S. Frey—p. 305.

Right Ventricle Puncture During Venous Air Embolism.—Frey says that, although ventricular puncture had been largely given up as treatment for venous air embolism, two recent reports about the alledgedly successful treatment of air embolism by ventricular puncture call for reinvestigation. He cites animal experiments which indicate that air is found in the right side of the heart when large quantities of air have been injected intravenously, not because of failure of the heart as the result of air filling, but because the pulmonary vessels are blocked by a part of the air and the escape of the remainder of the air is mechanically prevented. The author explains death as the result of venous air embolism in the following manner. Air which reaches the right side of the heart through a vein is driven in the form of bubbles into the pulmonary artery. These bubbles remain in the branches of the pulmonary artery. If complete blockage of the pulmonary circulation is produced by the air bubbles, death results, because the organism receives no oxygen (asphyxiation). Blockage of a large part of the lung (about two thirds) likewise causes asphyxiation, but if blockage of the circulation is such that an adequate amount of blood can still be oxygenated, then mechanical impairment of the heart action by the blockage in the pulmonary circulation may result in death (heart death). The clinical course of air embolism depends not so much on the quantity of air but on the rapidity with which it enters the circulation. Enormous quantities of air can be injected into animals without unfavorable effects, provided the injection is made slowly, because then the air enters the right heart in small bubbles and is driven into the small ramifications of the pulmonary artery, so that only small parts of the lung become blocked. If the air enters rapidly and large bubbles enter the heart, these large bubbles block the large branches of the pulmonary artery and completely interrupt the pulmonary circulation. This explains also why entrance of air into veins close to the heart leads to rapid death, whereas air in peripheral veins is comparatively harmless. In some cases air embolism causes no clinical symptoms, in other cases symptoms such as dyspnea, palpitation, piercing pains in the chest, anginal pains and vertigo rapidly disappear. In fatal air embolism death may be sudden or protracted. The breathing of oxygen and the intracardiac injection of epinephrine are the most effective methods in air embolism. The aspiration of air from the right side of the heart by means of percutaneous puncture is not advisable, because it is based on a mistaken assumption. The author analyzes the aforementioned two cases and questions the life-saving effect of cardiac puncture.

Deutsche medizinische Wochenschrift, Stuttgart

75:815-846 (June 16) 1950. **Partial Index**

Late Results of Surgical Removal of the Spleen. H. Schönlebe.—p. 823.
*Does Typhus Produce Life-Long Immunity? F. von Bormann.—p. 826.
Results of Ultrasonic Wave Therapy in Rheumatic and Degenerative Diseases of Joints. W. Zinn and V. Sonnenschein.—p. 827.
Experiences with Antabuse in Treatment of Chronic Alcoholism. R. Goblet. —p. 831.
*Testosterone in Treatment of Incurable Carcinoma of Female Genitalia. H. Burger and H. Drescher.—p. 835.

Immunity After Typhus.—According to von Bormann, of 259 inhabitants of a Russian village who had had typhus 10 or 20 years previously, 66 (about a fourth) contracted typhus a second time. Only 11 of these second attacks had an abortive course; 15 were severe. There were no fatalities. In the adult inhabitants who did not have typhus previously, the morbidity

was 52 per cent. The author concludes from this that, although an attack of typhus confers protection, it does not confer lifelong immunity.

Testosterone for Incurable Carcinoma of Female Genitalia.—Burger and Drescher state that 20 women with incurable carcinoma of the genitalia were treated with testosterone propionate at Women's Clinic of the University of Tübingen. Irradiation was usually continued during the time the male hormone preparation was given. Some patients were given, in addition, so-called mitosis toxins, such as arsenic, nitrogen mustards, colchicine or choline. Improvement was observed in 13 patients who were treated with doses of 100 to 400 mg. of testosterone propionate. The general condition improved, pain subsided, the appetite improved and some showed an increase in weight and a decrease in menopausal symptoms. Although the fatal outcome could not be prevented, life was prolonged in some instances. The hormone treatment failed in two cases.

Klinische Wochenschrift, Heidelberg

28:385-424 (June 15) 1950. **Partial Index**

*Second Hormone of Carbohydrate Metabolism Produced in Pancreas (Glucagon): Its Production by Alpha Cell System. K. Gaede, H. Ferner and H. Kastrup.—p. 388.
Toxic Effects Caused by Treatment with Nitrogen Mustards. E. Gadermann.—p. 394.
Use of Stilbamidine in Generalized Plasmocytoma. H. Goldeck.—p. 399.
Recurring Tonsillitis. A. Jonasch.—p. 407.
Acid-Base Equilibrium in Blood of Persons with Chronic Malnutrition. E. Dunker and H. Gardemann.—p. 412.
Sugar Values of Normal Cerebrospinal Fluid During Fractional Withdrawal. H. Weise.—p. 416.

Pancreatic Glucagon.—Gaede and his co-workers direct attention to the so-called paradoxical effect of insulin, which consists in a mild increase in blood sugar immediately before the hypoglycemic effect of insulin becomes manifest. A substance which is glycogenolytic and increases blood sugar has been isolated as the result of careful chemical preparation of pancreas from horses and of substances remaining after the extraction of insulin from cattle and swine pancreas. This pancreatic substance, which has been designated a glucagon, is a pancreatic hormone. The pancreas contains three systems. The excretory system produces digestive enzymes as well as lipotropic substances, which Dragstedt designated a "lipocaic" and which is probably identical with what Gavin, Patterson and McHenry termed inosit. The beta cells of the pancreas produce insulin. To determine what part of the pancreas produces glucagon, the antagonist of insulin, which increases blood sugar, the exocrinic portion of the pancreas was destroyed in a dog by ligation of the excretory ducts. Subsequently, the beta cells were destroyed in this animal by the injection of alloxan. This turned the pancreas into a connective tissue body which, besides small remnants of atrophic lobules, contained only alpha cells. Extracts of this gland had only the effect of increasing the blood pressure. It appears, therefore, that the increasing blood pressure factor glucagon, originates in the alpha cells. The role of these cells and the insulin-producing beta cells in the regulation of the carbohydrate metabolism is discussed. Insulin reduces the blood sugar content and promotes the synthesis of glycogen; glucagon, on the contrary, increases the blood sugar and promotes the decomposition of glycogen. Glucagon produces glucose, and insulin further oxidizes it. This probably explains why both hormones have an antiketogenic effect. The alpha cell system probably plays a role in the reaction of the organism to insulin and might cause, or at least influence, the tendency to acidosis observed in some diabetic patients. It is probable that glucagon is responsible for the distinctive characteristics of certain forms of diabetes.

Medicina, Buenos Aires

10:157-210 (June) 1950. **Partial Index**

*Site of Formation of Renin in Kidneys. A. C. Taquini, J. C. Fasciolo and D. Fernández Luna.—p. 174.
*Diabetes Mellitus in Infant Five Months Old. J. C. Recalde Cuestas, J. J. Staffieri and P. O. Tommasino.—p. 185.

Place of Formation of Renin in Kidneys.—Taquini and collaborators made quantitative determinations of renin in the kidneys of dogs, cats and pigs. They used a method which permits measurement of this substance in minute quantities in renal tissue. They found that renin is either produced or stored in the convoluted tubules in the outer layer of the renal cortex. The results did not indicate whether the proximal or the distal segments of the convoluted tubules play the predominant role in the formation or storage of renin.

Diabetes Mellitus in Infant.—Staffieri and Tommasino report diabetes mellitus in a five month old infant; they believe this to be the first in the Argentine medical literature. There was neither obesity nor diabetes in the family. The infant did not have any infectious process before the appearance of diabetes. The diet had to be approximated as far as possible to a normal diet suitable for a patient of this age. The disease caused acute toxic symptoms. The liver was enlarged. The treatment consisted of 5 units of insulin given every four hours. The daily maintenance dose of insulin was reduced to 8 units, given in two doses of 4 units each.

Pediatria, Naples

58:153-244 (March-April) 1950. **Partial Index**

*Aureomycin and Chloramphenicol in the Treatment of Whooping Cough. L. Barbera and G. Marchese.—p. 177.
*Combined Penicillin and Synthetic Antihistamine in Treatment of Glomerulonephritis in Children. V. Baffi.—p. 198.

Aureomycin and Chloramphenicol in Whooping Cough.—Barbera and Marchese treated 18 children with whooping cough with aureomycin and chloramphenicol. A dose of 50 mg. a day of either drug per kiligram of body weight was administered four times in 24 hours for five to eight days. There was a definite improvement in every case as evidenced by the lessening of the number and intensity of paroxysms, rapid recovery of the general health and return of sleep and appetite. The earlier treatment was started, the more pronounced these results. Suckling infants benefited most from the treatment. With the exception of a mild intolerance toward aureomycin in some of the youngest children there was no difference in the therapeutic effect of the two drugs.

Combined Penicillin and Antihistamine in Glomerulonephritis in Children.—Baffi reports five cases of glomerulonephritis in children between the ages of 2 and 10 years. The disease in all cases was due to a pharyngeotonsillar infection. The combined treatment consisted of administration of penicillin and of antihistaminic drugs. Penicillin was given by the intramuscular route every three hours in a daily dose of 160,000 units for 10 to 20 consecutive days. The antihistaminic drug was given in daily doses of four or five tablets of 0.10 Gm. each in the course of penicillin treatment and for five days more after discontinuation of penicillin. The disease was controlled in the first week of treatment. The author concludes that the combined treatment gives better results than either penicillin or antihistaminic drugs alone.

Praxis, Bern

39:607-646 (July 20) 1950. **Partial Index**

Development of Pediatrics in Switzerland. E. Feer.—p. 609.
Clinical Aspects of Acute Water and Electrolyte Disturbances in Infants: Toxicosis with Hyperelectrolytemia, Hypopotassemia and Masked Chloride Deficiency in Infant 2 Years Old. G. Fanconi and A. Prader.—p. 611.
Hypertrophy of Pylorus in Suckling Infant. M. Jaccottet and R. Jaccard.—p. 614.
Pituitary Adrenocorticotropic Hormone (ACTH): Experimental and Clinical Study. R. S. Mach and P. Ducommun.—p. 618.
*Clinical Aspects and Problems of Polyradiculitis in Childhood (Guillain-Barré Syndrome). E. Glanzmann.—p. 622.

Clinical Picture and Problems of Guillain-Barré Syndrome.—Glanzmann reports nine cases of Guillain-Barré syndrome in children. The syndrome occurred as an idiopathic disease in a girl aged 4; it was associated with encephalomyelitis after measles in a girl aged 7, and with Landry's paralysis in a girl aged 2. One girl aged 11, who had had poliomyclitis at the age of 7, had Landry's paralysis with a complete recovery. It seems likely that her first as well as her second disease was a Guillain-Barré syndrome, since allergic reactions have a tendency to recur. Two brothers aged 1 and 4 years had erythredema polyneuropathy associated with Guillain-Barré syndrome. One girl aged 4 had erythredema polyneuropathy and polyradiculitis, which presented itself as a febrile, intercurrent, secondary infection. Radiculitis with great increase in the pro-

tein in the cerebrospinal fluid, without a corresponding increase in cells, occurred, during an epidemic of poliomyelitis, in a boy aged 4 after severe gastroenteritis. One boy aged 6 with megasigmoid had amyotrophic polyneuritis associated with Guillain-Barré syndrome which was probably due to a deficiency of vitamin B_1 caused by an abnormal bacterial condition in the intestine. The epidemic occurrence of polyradiculitis with or without simultaneous epidemic of poliomyelitis, the occurrence of polyradiculitis in siblings and the sporadic occurrence of polyradiculitis independent of any other disease suggests that a specific neurotropic virus may possibly be the causative agent. Polyradiculitis could be considered as a sister disease of poliomyelitis, the relation being similar to that of parapertussis and true pertussis. Polyradiculitis can be differentiated from poliomyelitis by the clinical picture.

Presse Médicale, Paris

58:937-948 (Sept. 2) 1950

New Toni-Cardiac Substance: Crystallized Thevetin. C. Lian and A. Kursat.—p. 937.
New Studies on Mushroom Poisoning. L. Binet, M. Leblanc and G. Wellers.—p. 938.
*Hemolytic Disease in Newborn Due Only to ABO Incompatibility, Successfully Treated with Transfusion of O-Erythrocytes and AB-Plasma. R. Seigneurin, J. Roget, J. Groulade and F. Viallat.—p. 939.

Hemolytic Disease in Newborn Due only to ABO Incompatibility.—Seigneurin and co-workers report an infant boy born at term, his parents' second child, with icterus occurring several hours after birth and becoming severe within the succeeding 24 hours. The Rh factor was not responsible for the icterus, since the father was B Rh positive, the mother O Rh positive and the infant B Rh positive. Determination of the ratio of the regular agglutinins in the mother's serum showed an abnormal increase in anti-B agglutinins (1:2048). Erythroblastosis and leukocytosis in the infant resulted from maternal isoimmunization to hemoagglutinogen B. This also caused the passing of anti-B antibodies into the milk of the mother in the same high ratio as in the mother's serum. The infant was given three transfusions of 100 cc. of blood into a fontanel. The first transfusion was given 38 hours after birth, the second 18 hours later and the third on the twelfth day of life. The transfused blood was artificially composed of O erythrocytes in suspension in AB plasma. The mother's milk was withheld from the infant. The icterus became less severe on the third day and disappeared completely on the ninth day. Erythroblastosis and leukocytosis subsided, and the number of red blood corpuscles increased. The infant was apparently cured when it was discharged from the hospital on the twentieth day.

Revista Brasileira de Cirurgía, Rio de Janeiro

19:471-564 (May) 1950. **Partial Index**

*Surgical Treatment of Pulmonary Tuberculosis: Upper Partial Thoracoplasty. Based on Results in 577 Thoracoplasties. E. J. Zerbini and M. Alves Lima.—p. 489.

Surgical Treatment of Pulmonary Tuberculosis.—Zerbini and Alves Lima performed 577 partial thoracoplasties in 333 patients with pulmonary tuberculosis. The disease was unilateral in 150 cases and bilateral in 183. The contralateral lesion in the latter group was controlled after (unilateral) thoracoplasty by pneumothorax in 87 patients, by pneumothorax and Jacobaeus' operation in 15, by pneumothorax with crushing of the phrenic nerve in five, by extrapleural pneumothorax in two and by bilateral thoracoplasty in three; the contralateral lesion healed spontaneously in 71 patients. The cavity in these patients had a diameter of less than 3 cm. in 83, of more than 3 cm. in 193 and of more than 8 cm. in 57. Thoracoplasty was performed in only one stage in 111 patients, in two stages in 197, in three stages in 10, in four stages in three. Upper partial thoracoplasty resulted in cure in 174 patients (52.5 per cent) between one and 13 years after the operation. The operation is likely to fail because of the coexistence of pulmonary and bronchial tuberculosis. A roentgenologic and bronchoscopic diagnosis of bronchial tuberculosis is important. Treatment of the pulmonary lesion, when both types are present consists of a cavernoscopy, when the general condition of the patient is poor, and of lobectomy or pneumonectomy, if the general condition of the patient makes the operation advisable.

Schweizerische medizinische Wochenschrift, Basel

80:783-806 (July 29) 1950

Prefrontal Leukotomy. G. Condrau.—p. 783.
Results of Studies on Fine Structure of Urinary Calculi of Patients from the Near East. W. Epprecht and H. R. Schinz.—p. 792.
*Myocardosis Associated with Cirrhosis of Liver. M. Oppenheim.—p. 795.
Angiocardiopneumography in Diagnosis of Tumors of Lung and Mediastinum. M. Battezzati, F. Soave and A. Tagliaferro.—p. 799.

Myocardosis Associated with Cirrhosis of Liver.—Oppenheim reports cirrhosis of the liver in 128 men and 40 women. Seventy-eight of the patients (57 men and 21 women) died, and necropsy was performed. Signs of myocardosis were observed in a considerable number of the living patients and in all the fatal cases. Pathological conditions of the blood proteins were observed in practically all. A positive Weltmann reaction, increased sedimentation rate of blood, positive cadmium reaction, lowering of total protein ratio and increase of alkaline phosphatase were the most frequent and constant pathological signs in the living patients and in the fatal cases, but these signs were more frequent and more pronounced in the fatal cases. Definite correlation was observed between the severity of the anatomic disease, the disturbance of the protein chemistry, the pathological electrocardiograms and the course of the disease. There were twice as many patients without hypoproteinemia who survived as there were patients without hypoproteninemia who died, while the number of patients with hyproteinemia who survived equaled the number that died. Fatal cases were less frequent among patients with normal electrocardiograms. Hypoproteinemia proved to be first and the pathological electrocardiogram second with respect to prognostic significance. There exists a reciprocal effect between dysproteinemia, particularly hypoproteinemia, and myocardosis, in that the hypoproteinemia contributes considerably to the development of myocardosis. Since hepatic lesions are manifested by dysproteinemia, the myocardosis associated with cirrhosis of the liver should be considered a hepatogenic disease of metabolism of the myocardium.

Semaine des Hôpitaux de Paris

26:2915-2950 (Aug. 18) 1950

*Nephro-Omentopexy: Therapeutic Results. J. C. Rudler and J. Cottet.—p. 2915.
Observations Concerning Bronchoscopic Topography and Catheterization of Bronchial Orifices. G. Arnaud and J. Ioannou.—p. 2923.
Capillary Hyperpermeability: Treatment in Post-Traumatic Local Reflex Syndromes. H. Laborit.—p. 2930.

Nephro-Omentopexy.—Rudler and Cottet performed nephro-omentopexy on 13 patients, 12 of whom had typical nephroangiosclerosis with retention of urine and albuminuria; one had acute nephritis in the phase of transition to chronic nephritis with hypertension. Ten of the 12 patients with nephroangiosclerosis were hypertensive. Urinalysis and renal function tests were done before the surgical intervention. Thus a definite functional difference was frequently revealed in the two kidneys. Surgical intervention was performed on the kidney whose function was impaired to a greater extent. Catheterization of the kidneys was repeated three to six months after intervention. The function of the kidney operated on was equal or superior to that of the other kidney. Two patients died of anuria within the first six postoperative days. Five additional patients died within three months to two and a half years after operation, three of them from cardiac failure. Two more patients died within three years and three months after the operation. Two of the four surviving patients were subjected to bilateral nephro-omentopexy. The preoperative blood urea levels of 1.05 Gm. and 1 Gm., were reduced to about 0.50 Gm. in these two patients. The phenolsulfonphthalein excretion was reduced to 25 per cent in the first of these patients, and fatigability, headache and digestive disturbances were improved in the second patient. Cardiac decompensation and blood urea above 1.80 to 2 Gm. are definite contraindications of nephro-omentopexy. One should perform renal function tests and catheterization in order to avoid surgical intervention in a phase of an ascending uremic bout and also to

prevent the risk of operating on the only kidney which may still have some of its function while the other is no longer functioning. Nephro-omentopexy did not aggravate the renal function in any of the authors' cases, although all of them were severe. Ureteral catheterization showed that the kidney operated on was improved as compared to that not operated on. It seems necessary that both kidneys be operated on. Although nephro-omentopexy is not the ideal treatment for chronic nephroangiosclerosis, it may induce improvement in patients whose condition is not so severe. Arterial hypertension and albuminuria are not benefited by nephro-omentopexy.

Ugeskrift for Laeger, Copenhagen

112:919-948 (June 29) 1950. **Partial Index**

*Effect of ACTH and Cortisone in Rheumatic Fever. A. Videbaek, G. Asboe-Hansen, P. Astrup and others.—p. 919.
Importance of Cultivation of Gonococci from Rectum in Women. K. Bülow.—p. 929.

ACTH and Cortisone in Rheumatic Fever.—Videbaek and his associates report that treatment with pituitary adrenocorticotropic hormone (ACTH) gave remarkably good clinical results in a girl, aged 15, with a first acute attack of rheumatic fever and in a woman, aged 28, with fever and joint disorder of almost a year's duration. It had more doubtful effect in a youth, aged 16, who also had a first acute attack of rheumatic fever and in whom earlier treatment with cortisone was without noteworthy result. Temperature and pulse rate improved strikingly in all patients. The general condition was noticeably better. The pronounced exudative pericarditis in the first patient decreased rapidly during and after treatment; in the second patient, with pancarditis, there was some decrease in the heart shadow; in the third patient, with pericarditis, the heart shadow was not affected. In all patients there were moderate amounts of hyaluronic acid in the connective tissue before treatment, but none was demonstrable in the skin when the treatment was terminated. Reduced healing power in wounds was noted in one instance. Complicating infections developed in two patients.

112:985-1006 (July 13) 1950

*Mortality and Danger of Cancer of Stomach in Patients with Pernicious Anemia. J. Mosbech and A. Videbaek.—p. 985.
Two Cases of Secondary Intestinal Tuberculosis Treated with Para-aminosalicylic Acid. O. Jensen.—p. 991.

Cancer of Stomach in Patients with Pernicious Anemia.—Mosbech and Videbaek say that of the 301 patients with pernicious anemia (219 women, 82 men) treated in Bispebjerg Hospital from 1928 to 1949, 224 were observed for more than 10 years. Follow-up of these cases showed that life expectancy for women who were treated for pernicious anemia is the same as that of the normal population and that for men there is a slightly but not significantly higher mortality. Of the total number of patients, 115 (83 women, 32 men) were dead. Twenty-one patients died from cancer, which corresponds to the expected number of deaths from this disease, but no less than eight women and seven men had cancer of the stomach. The higher incidence of cancer of the stomach in the men is difficult to explain. There was no evidence that the men were alcoholics. The investigation confirms that patients with pernicious anemia have a special predisposition to cancer of the stomach. This is attributed not so much to the pernicious anemia in itself as to the fact that these patients have achylia.

112:1007-1040 (July 20) 1950. **Partial Index**

Vinyl Ether Alone or in Combination with Ether Anesthesia in Adenotomy and Tonsillectomy. T. Strange.—p. 1012.
*Inoculation Hepatitis in Patients Treated with Dry Serum. G. Kjaergaard.—p. 1014.
Functional Training in Flat Foot. S. O. Brandt.—p. 1018.

Inoculation Hepatitis in Patients Treated with Dry Serum.—Kjaergaard says that follow-up of 542 patients treated with Danish pooled dry serum and observed for at least seven months revealed that in 23 (3.87 per cent) hepatitis occurred which might be attributable to inoculation with hepatitis virus during hospitalization. In a control group hepatitis occurred in 0.64 per cent. In the general population the incidence of hepatitis during the same period was between 0.3 and 0.4 per cent. The two groups of patients, however, are not directly comparable, and that the jaundice was caused by the serum infusions alone is regarded as doubtful. The frequency of hepatitis in the patients treated with dry serum corresponds closely to that reported by Marcussen in patients treated only with intravenous injections.

Wiener klinische Wochenschrift, Vienna

62:381-396 (June 2) 1950. **Partial Index**

*Usefulness and Hazards of Treatment of Typhoid and Paratyphoid Fever with Chloramphenicol (Chloromycetin®). P. Mollaret.—p. 381.
Early Diagnosis and Estimation of Chances of Treatment of Cancer of the Stomach. R. Boller.—p. 384.
Endometriosis of Urinary Bladder and Estrus-Producing Compounds. H. Siegmund.—p. 387.
*Forty Cases of Progressive Peritonitis After Perforation of Appendix Without Fatality. J. Eberle.—p. 389.

Chloramphenicol in Typhoid and Paratyphoid Fever.—Mollaret treated 100 patients with typhoid and paratyphoid fever with chloramphenicol (chloromycetin®). Treatment was instituted with an initial dose of 2 or 3 Gm. Maintenance doses of 0.25 or 0.50 Gm. were administered in capsules every three hours. The temperature was lowered within one or two days, reaching 98.6 F. (37 C.) within about four days. Headache, listlessness and insomnia disappeared within 48 hours. Diminution in the size of the spleen was observed within four to five days. Digestive disturbances showed a somewhat slower response. Cultures of blood and of feces rapidly became negative. There were recurrences in 15 patients. Intestinal hemorrhages occurred in seven patients and intestinal perforation in one. Venous thrombosis developed in three patients in the course of the treatment. Encephalitis was observed in nine patients and jaundice in two. Death from circulatory collapse occurred in two patients. Necropsy revealed lesions similar to those which were observed in guinea pigs after the injection of typhoid endotoxin. The author believes that the drug exerts an indirect toxic effect by the massive liberation of endotoxin through the massive disintegration of the bacteria. Psychic disturbances, such as agitation, hallucinations and depression, were observed in all patients but subsided rapidly except in two patients who had to be transferred to the psychiatric ward for a prolonged period. Experience in the two fatal cases induced the author to desist from the initial dose and to use maintenance doses of 2 or 3 Gm. of the drug within 24 hours. Treatment should begin with smaller doses even in the patient in the advanced stage of the disease whose organism probably has been saturated with endotoxin. Treatment should be discontinued temporarily, for two or three days, in patients with subnormal blood pressure with a tendency to lowering of the differential pressure, acceleration of pulse and too rapid drop in temperature on the second or third day of the treatment.

Spreading Peritonitis After Perforation of Appendix.—Eberle reports 40 patients, 19 adults and 21 children, with spreading peritonitis due to perforation of the appendix. Operation was done with ether inhalation anesthesia in the majority of the cases. Exposure, isolation and removal of the appendix was carried out with as little trauma as possible, so that reparative walling off processes were not interfered with. Mopping and suctioning was done in the cecal area, but the abdominal cavity was not irrigated. A 5 mm. rubber drain was inserted in the wound, and peritoneum, muscles and fascia were closed tightly. One Gm. of streptomycin, 100,000 to 200,000 units of penicillin and 6 Gm. of sulfacetamide in 50 cc. of isotonic sodium chloride solution were injected through the drain, which was then removed. Continuous drip infusion was given for 48 hours, but as a rule sulfonamide compounds or antibiotics were not administered after the operation. However, two patients with perforation of a cecal abscess were given 0.25 Gm. of streptomycin every six hours and 40,000 then 20,000 units of penicillin by parenteral route every three hours for several days. Temperature was restored to normal within a few days; the boardlike hardness of the abdominal muscles subsided on the second or third day, and intestinal function was restored rapidly. There were no fatalities. Complete recovery occurred in 10 to 14 days. Douglas' abscess developed in two cases, requiring incision in one. No other complications were observed.

BOOK NOTICES

The reviews here published have been prepared by competent authorities and do not represent the opinions of any official bodies unless specifically stated.

Voluntary Prepayment Medical Care Plans. Revised 1950. Paper. Pp. 137. Council on Medical Service, American Medical Association, 535 N. Dearborn St., Chicago 10, 1950.

This is the most current revision of an annual publication inaugurated by the Council on Medical Service in 1946. It is designed primarily for those who are interested in a summary description of the organization, benefits and costs of the many voluntary health insurance programs in operation. The original edition listed 45 plans operating in 27 states and the Territory of Hawaii. That edition included only those plans sponsored by medical societies and/or coordinated with local hospitalization plans. Each succeeding revision has listed an increasing number of plans. The current revision lists 78 such plans operating in 45 states, the District of Columbia and Hawaii. In addition, this issue lists other types of plans domiciled and operating in the Dominion of Canada. A three page table of contents lists the plans by states and by sponsorship. The introduction relates the early development of health insurance plans under medical sponsorship and also makes reference to early actions of the House of Delegates. Since voluntary health insurance is evolutionary, the introduction contains an explanation of some of the current experiments in this important field. Part 2 defines many of the terms used in explaining the various phases of these plans. Part 7 contains a summary depicting the growth in number of plans, growth in enrolment, a brief description of the various types of plans and the different methods of organization.

The Art of Real Happiness. By Norman Vincent Peale, D.D., and Smiley Blanton, M.D. Cloth. $2.75. Pp. 247. Prentice-Hall, Inc., 70 Fifth Ave., New York 11, 1950.

The authors, each well known in his field and author of previous successful books, have collaborated effectively in the production of this volume. They present a series of cases illustrating the commonest areas in which unhappiness occurs. The book opens with a discussion of new hope for a happier life, which the authors hold is possible for most persons of normal mentality. The love-hate duality is clearly defined and explained, together with the general principles underlying the attainment of peace of mind. Fundamental to the concept set forth in this book is the belief that there is a God from whom help can come if properly sought. From this premise, the authors have approached their cases in practice, and they so report them. The ability to relax after having done one's best, to stay healthy under pressure, to deal with depression (emotional) and anxiety, which are attributed mainly to guilt complexes, how to achieve a happy marriage (and to keep it that way), a solution for problem drinking, comfort in bereavement and the ability to grow older happily are all discussed optimistically yet realistically. The case report method and the solutions are clearly, interestingly and readably presented. The book can be recommended without reservation for lay readers whose problems fall within its scope.

Biological Actions of Sex Hormones. By Harold Burrows, C.B.E., Ph.D., F.R.C.S. Second edition. Cloth. $8.50. Pp. 615, with 8 illustrations. Cambridge University Press, Bentley House, 200 Euston Rd., London, N.W.1; American Branch, 51 Madison Ave., New York 10, 1949.

This is a coordinated summary consisting chiefly of laboratory studies on the biologic actions of the sex hormones in mammals. The treatise represents an exhaustive study thoroughly documented from the literature and from the author's experience of the effects of the gonadotropins, androgens and estrogens on living tissue and on the structure, function and behavior of the entire organism. As such, the book is chiefly of value to those conducting animal experimentation in this field or who require a source book.

Chirurgisch-gynäkologische Grenzfragen: Physiologie und Pathologie der weiblichen Geschlechtsorgane in Beziehung zur Chirurgie. Von Prof. Dr. Herbert Uebermuth. Half-cloth. 9 marks. Pp. 168, with 16 illustrations. Georg Thieme, Thomaskirchhof 21, Leipzig C 1, 1950.

This book deals with borderline cases in gynecologic surgery. Many so-called borderline questions are propounded, and an attempt is made to answer these, the answers being based on both statistical data and the author's experiences. The book is divided into the following three parts: part 1, dealing with the female cycle and borderline surgical questions; Part A of this section, the influence of menstruation on operative procedures, and Part B, intraperitoneal bleeding (gynecologic) as an indication for surgical intervention; part 2, pregnancy and the surgical borderline questions, and part 3, gynecologic diseases and borderline cases. The pros and cons of surgical intervention during menses are discussed, and various authorities are quoted. The author reports no complications in 126 major surgical procedures performed during menses. In 400 cases of intraperitoneal bleeding, only 55 were not caused by ectopic pregnancies; these 55 were of ovarian origin. In part 2 the author discusses hexobarbital sodium (evipan, evipal®) and ether anesthesia in cesarean section and states that the babies are born apneic when these are used.

The author stresses the point that infections, regardless of how slight, increase the possibility of abortion; therefore, abscesses and empyemas should be treated immediately. In cases of appendicitis associated with pregnancy, the author is opposed to conservative treatment even if an abscess has developed, and hence advocates early surgical intervention. He advises conservative treatment for six months after delivery in cases of "cholezystopathie." This term was confusing since it was not clarified. In gallbladder disease associated with pregnancy the author believes that surgery is indicated only if the patient's life is in danger, especially in those cases associated with common duct obstruction and empyema with impending peritonitis. Toxic diffuse goiter (Basedow's disease) is infrequent in pregnancy, and the author cites newer statistics showing an incidence of 0.2 per cent. Abortions, however, are frequent, occurring in 28.7 per cent of such cases. The book is well written and includes a few illustrative roentgenograms and microscopic sections. The subject of chemotherapy, however, should have been included. The book can be recommended as a reference for those interested in surgery and gynecology.

The Causation and Treatment of Delayed Union in Fractures of the Long Bone. By Kenneth W. Starr, O.B.E., E.D., M.B., Surgeon, Sydney Hospital, New South Wales, Sydney. (This Jacksonian Prize Essay is Published with the Kind Permission of the Council of the Royal College of Surgeons of England). Cloth. $9. Pp. 215, with 109 illustrations. Butterworth & Co., Ltd., 4-6 Bell Yard, Temple Bar, London, W.C.2; The C. V. Mosby Company, 3207 Washington Blvd., St. Louis 3, 1947.

In this relatively small book there is an enormous amount of information on the physiology and pathology of bone. Part 1, The Morphogenesis of Bone, includes discussions of the structure and chemistry of bone, a short history of the research in reconstruction, deposition and resorption of bone and the relation between structure and function in bone morphology. In part 2, The Healing of Fractures, the author discusses the anatomic structures involved in repair as well as the process of repair following fractures. Part 3, on the etiology and treatment of delayed union, includes statistics, adjuvant therapeutic methods, the principles and management of difficult fractures, the treatment of closed and open fractures, septic fractures and the skin problem. The bibliography indicates the extent of investigation of literature. The title of the book might result in underestimation of its contents. Actually, healing of the long bone fractures is dealt with in detail and from every aspect, and often what appears to be merely academically important is developed so that its practical significance in the study of delayed

union or nonunion is made evident. The style is pleasant, and the presentation is logical, so that the book is easy to read. The line of thought is clear throughout. Underlying the whole text is a vindication of the deductions of John Hunter, which seemingly have been obscured by clinical investigations of the past half century.

There appears to be little in the book which is original, but the author has succeeded in presenting some often forgotten observations in such a manner that the reader is made to realize the poverty of originality in research work done in the last few decades. The author has presented a challenge to modern orthopedists to add to the information which has been gathered about bone healing in recent centuries. It is an appeal for research of a more fundamental nature rather than complete dependence on clinical research, with its apparent limitations. The author is wont to blame the advent of radiography for this present day tendency.

The text is well illustrated, with numerous well chosen microphotographs and diagrams. The portion on treatment represents a report of a vast experience in dealing with all types of fractures. Some of the treatment is outdated. This is particularly true of the use of antibiotics, the knowledge of which has been increased so rapidly. The book is an excellent textbook for anyone interested in bone and joint surgery. It meets a long-felt need for a comprehensive treatment of the basic facts about growth and healing of bone.

Oxidation-Reduction Potentials in Bacteriology and Biochemistry. By L. F. Hewitt, Ph.D., B.Sc., F.R.I.C., Director, Serum Research Institute, Medical Research Council, Carshalton, Surrey. Sixth edition. Cloth. $4.50. Pp. 215, with 44 illustrations. The Williams and Wilkins Company, Mount Royal & Guilford Aves., Baltimore 2, 1950.

Formidable as the title appears, this volume contains, in addition to the technical procedures and definitions, much information which students of all the biologic sciences, including medicine, will find of practical value and interest.

Many biologic processes are either oxidation-reduction systems (i. e., involve exchanges of electric charges) or are affected by oxidation-reduction reactions. The chapter on Systems of Biological Interest includes discussions of sulfydryl systems, hemoglobin, several of the vitamins and hormones, as they are related to the subject. The chapter Bacteriological Applications covers many aspects of the electrode potentials developed and their effects on the metabolism of unicellular organisms. New chapters, not in the last edition, 1948, include applications of oxidation-reduction systems to p_H determinations, metabolic cycles of integrated enzyme systems and the mode of action of antibiotics and chemotherapeutic agents. The author presents the material in an interesting style seldom encountered in technical books, and the text is well annotated with extensive references.

Manual: Procedures and Layout for the Infant Formula Room. American Hospital Association M8-49. Paper. $1.50 to members; $2.25 to nonmembers. Pp. 52, with 3 illustrations. The Association, 18 E. Division St., Chicago 10, 1949.

This manual is designed to guide hospital executives in planning, installing, equipping and administering a formula room. It was prepared under the guidance and with the assistance of members of a committee appointed by the Council on Professional Practice of the American Hospital Association. The important hospital problem having to do with the prevention and control of diarrheal disorders requires, for its solution, the proper organization and operation of the formula room. Sufficiently detailed information is reported to make this a practical and useful guide. In the preparation of this manual the committee has made an important and useful contribution.

The Salt-Free Diet Cook Book. By Emil G. Conason, M.D., and Ella Metz. Cloth. $3. Pp. 137. Lear Publishers, 105 E. 15th St., New York 3; Distributed by Crown Publishers, 419 Fourth Ave., New York 16, 1949.

This book consists chiefly of a group of menus with estimates of sodium content. Usefulness of this book is limited basically by the fact that more information is needed for the development of truly representative figures for the sodium content of individual foods.

The Future in Medicine: The March of Medicine, 1949. Number XIV of the New York Academy of Medicine Lectures to the Laity. Cloth. $2.50. Pp. 160. Columbia University Press, 2960 Broadway, New York 27, 1950.

The five articles that make up this volume cover phases of medicine that embrace law, sociology, physics, criminology, hematology, immunology, anthropology and psychiatry, so that the general public and members of the medical profession may review important recent developments which unquestionably will influence the future in medicine. These essays have been prepared by renowned authorities in their field. Their contributions are provocative and worthy of reading by all who have an interest in medical affairs. The volume well deserves a place with the others that make up this series and should be handy in libraries or on the night table.

Rose's Laboratory Handbook for Dietetics. Revised and Rewritten by Clara Mae Taylor, Ph.D., Professor of Nutrition, Teachers College, Columbia University, New York, and Grace MacLeod, Ph.D. Fifth edition. Cloth. $5. Pp. 358. The Macmillan Company, 60 5th Ave., New York 11, 1949.

This useful book has been expanded to include the more recent quantitative data on food composition. It is intended for use by teachers, community and public health nutritionists, the hospital dietician, the advanced student of nutrition, doctors interested in nutrition and any other persons who may be interested in the quantitative aspects of the national food supply and its nutritive value.

Part 1 includes a brief discussion of functions of food and food requirements for different age groups during various activities. Part 2 consists of common problems in dietary calculations. Reference tables make up part 3. These tables include such useful data as equivalents for weights and measures, vitamin equivalents, weight-height age tables for various age groups and conversion tables for common measures. Part 4 includes many tables of food composition. These tables give protein, fat, carbohydrate and caloric values for many common foods, along with such values as essential amino acids, minerals, oxalic acid, vitamin D, niacin, biotin, choline, pantothenic acid, paraaminobenzoic acid and pyridoxine. There is also in this section a useful table of approximate vitamin losses in cooking foods. For the most part this book is composed of tables and charts, which, although there is some repetition of data, appear entirely adequate. It also contains the necessary material to give the reader a basic understanding of the text.

Speech Problems of Children: A Guide to Care and Correction. Edited by Wendell Johnson, Ph.D. Prepared for the National Society for Crippled Children and Adults, by the American Speech and Hearing Association. Cloth. $3.75. Pp. 265, with 4 illustrations. Grune & Stratton, Inc., 381 4th Ave., New York 16, 1950.

Prepared according to a carefully developed plan to insure an authoritative approach, this book is the product of 11 authors under the editor. Included in the routine was a survey of each chapter by two professional consultants. As a result, the reader is assured of receiving information that can be considered accurate and generally acceptable, although, as is acknowledged, not all schools of thought regarding some aspects are necessarily represented.

The general problem of speech difficulties is broken down into its most important components. Included are chapters on functional disorders of articulation, speech retardation, cleft lip and cleft palate, cerebral palsy, hesitant speech, children of foreign tongues and children with impaired hearing. The general problem is clarified in the opening chapter, a survey by Frank P. Bakes, Ph.D., and there are general chapters on speech as it is acquired in the average home and in school surroundings. After each of the chapters dealing with specific subjects there is an adequate list of references. Interesting features are inclusion in the introductory section of a special message to parents and "A Word to All Concerned," in which general orientation is provided. Although directed perhaps primarily to parents, the volume contains material of equally great interest to social workers, nurses, teachers and physicians. The National Society for Crippled Children and Adults and the American Speech and Hearing Association are to be congratulated on having made an important contribution to better and more general understanding of speech problems and their solution.

Psychology and Mental Health: A Contribution to Developmental Psychology. By J. A. Hadfield, M.A., M.B., Ch.B. Cloth. $2.75. Pp. 444. The Macmillan Company, 60 5th Ave., New York 11; George Allen & Unwin, Ltd., Ruskin House, 40 Museum St., London, W.C.1, 1950.

This book reflects the concepts and practice of an experienced worker in the field of medical psychology, as well as the substance of certain lectures given by him in the course of 20 years at the University of London. The author deals primarily with psychopathology and the causes of mental disorder, as they relate to mental health. He confines himself to that segment of psychiatric inquiry pertaining to the psychoneuroses and behavior disorders, since in his judgment these are derived for the most part from environmental conditions and are therefore more accessible to prevention and cure than the more constitutionally determined psychoses. He lays special emphasis on predisposing causes in early childhood and on the psychology of the individual. He believes that by working out in the individual the causes of disorder and breakdown, clues may be found to causes of neurosis and unrest in the community.

The author's approach is dynamic, influenced by the teachings of Freud, Jung and Adler, but considerably modified by convictions based on his clinical practice. It is his thesis that the basic cause of the psychoneuroses is the feeling of deprivation of love, the need for protective love and security being in fact of far greater importance than repressed sexuality. This feeling of deprivation gives rise to morbid reactions—anger, self pity, hate, power fantasy, depression and pride—which are then repressed in favor of a moral superego, with resulting dissociation of personality and the emergence of psychoneurotic symptoms. The author attempts to show how this mechanism operates in the major clinical pictures—psychosomatic disorders, traumatic neuroses, hysteria, anxiety states, anxiety hysteria, obsessional neuroses, personality disorders and sex perversions and aberrations. In the process of treatment, he accepts in the main Freud's concepts of conflict, repression and projection and the use of free association. Free association, rather than dreams, is the gateway to the forgotten past. He avoids the process of transference as being neither necessary nor desirable and concentrates on direct, reductive analysis. This consists of going back to the original experience which gave rise to the repressed emotions, releasing the latter toward the person or experiences to whom or to which they properly belong, with subsequent redirection to useful ends. This is a provocative and rewarding book, effectively organized and presented, which contributes much to the cause of a more practical, middle-of-the-road, analytic psychiatry.

Sexual Fear. By Edwin W. Hirsch, B.S., M.D., Attending Urologist, Englewood Hospital, Chicago. Cloth. $3. Pp. 307. Garden City Publishing Co., Inc., Garden City, New York; 14 W. 49th St., New York 20, 1950.

Because the author uses a hopeful, encouraging approach in the chapters dealing with specific sex-linked fears, this book is well suited for the average lay reader. In the first six chapters, sex life and the development of sexual fears are traced historically from Babylonian days down through the Middle Ages to provide a background of understanding in relation to modern attitudes on sex. The first widespread recognition of syphilis with the siege of Naples in 1494 is described in an interesting discussion that includes other theories regarding the actual origin of this venereal disease.

Considered in the next six chapters are subjects of common discussion and all too frequent misunderstanding, including frigidity, the male change of life and impotence, this last chapter being enlivened with numerous specific case reports presented in nontechnical terms. This method is employed to some extent also in the final chapter, treatment of sexual fear by psychomatics, a term coined by the author to designate his system of investigating and correcting disordered sexual function due primarily to sexual fear. Psychomatic refers, Hirsch explains, not only to the mind, body and environment but also to "influences" outside and within the self. An extensive bibliography is provided for the reader interested in source material. Physicians should find this volume satisfactory for recommendation to patients with sexual maladjustments. It does an effective job of correcting the many ignorant conceptions concerning sexual function.

Genito-Urinary Surgery. By Sir John Thomson-Walker, D.L., M.B., C.M.Ed., Consulting Urologist, King's College Hospital, London. Third edition edited by Kenneth Walker, M.A., M.B., B.C., Urologist, Hornsey Central and Dartford County Hospitals, London. Cloth. $15. Pp. 956, with 340 illustrations. Paul B. Hoeber, Inc., Medical Book Department of Harper & Brothers, 49 E. 33rd St., New York 16, 1950.

This has been regarded as an outstanding textbook in urology since it was first published in 1914. The author was one of the most competent urologists of his time, and his thorough knowledge and wide experience are well reflected in the pages of this book. The present edition maintains the general excellence of the original volumes. Although the editor has attempted to bring the material up to date, it is evident that many of the recent developments in urology have not been included. It will be noted that but few of the references given at the end of the chapters were dated after 1935. This deficiency is apparent in the chapter on genitourinary infection and its treatment. There should be a more extensive discussion on the use of sulfonamides and the antibiotic preparations now in common usage. The chapter on the various methods of prostatectomy is inadequate. A more complete consideration of recent developments in this field, including transurethral prostatic resection, would be desirable. Errors may be noted in the discussion of the historical development of several urologic procedures, as, for example, in the origin of excretory urography. The book remains as one of the standard textbooks in urology and deserves a place in a representative medical library.

Die Leptospirose: Eine kurze Darstellung für Ärzte, Tierärzte und Gesundheitsbehörden. Von Prof. Dr. med. W. Rimpau. Monographien der "Medizinischen Klinik," Heft 8. Paper. 10 marks. Pp. 157, with 15 illustrations. Urban & Schwarzenberg, Thierschstrasse 11, Munich 22; Meinekestr. 13, Berlin W. 15, 1950.

This monograph contains an introduction and chapters on the morphology and biology of the Leptospiras; immunology, distribution, clinical aspects, pathology, epidemiology, and prevention and treatment of leptospirosis. The first part of the book, which is devoted to the causative organisms, contains much valuable information on observations made in central Europe and, before the war, in the Far East, while North American, Spanish, Latin-American and postwar Dutch publications are either disregarded totally or utilized only to a small extent. The clinical picture of leptospirosis is classified as leptospiral fever, renal form, hepatic form, meningitis, hepatorenal syndrome, bronchopneumonic form and the questionable chronic form. Fifteen fever curves illustrate the course of the disease. The symptomatology and pathology of the disease are discussed to some length without any reference to information available in standard American texts. The chapter on epidemiology contains a number of interesting observations made in Germany and Switzerland, especially on the relation of soil, temperature, moisture and leptospirosis in animals. The therapeutic recommendations are up to date, although one could add much to the description of prophylactic measures. The book was carefully printed on good paper.

Researches on the Radiotherapy of Oral Cancer. By Constance A. P. Wood and J. W. Boag. Medical Research Council, Special Report Series No. 267. Paper. 12s.6d. Pp. 148, with 77 illustrations. His Majesty's Stationery Office, York House, Kingsway, London, W.C.2, 1950.

This is a special report of a study of the Radio-therapeutic Research Unit. The purpose of the study was to compare the effectiveness of a radium beam unit with roentgen therapy at 185 to 200 KV in causing tumor regression. The report is in three sections. The first section compares the results of treatment with the beam unit and roentgen therapy of cancers of the mouth and throat. A number of patients were treated on one side with the beam unit and on the other with the roentgen therapy unit, for comparison of the skin reaction in the same patient. The second section deals with serial biopsies of oral carcinoma as an aid in obtaining prognosis and response to radiotherapy. The third section presents a statistical analysis of the response to treatment of 641 patients treated in the unit who were suffering from cancer of the mouth and throat. A statistical method of estimating the final results of a clinical experiment before long term survival figures become available is also described. The report is well written. Detailed data are given on the

content of the studies. It should serve as an excellent reference. Numerous figures and tables are included. Of the 30 plates, four are in color. One of the author's conclusions is that, if the glandular region were to receive a dose of the same order as the primary lesion, the glands would offer no greater resistance to irradiation than the primary lesion.

Administration of Schools of Nursing. By Dorothy Rogers Williams, M.A., R.N., Lecturer, Administrator of Schools of Nursing and Nursing Services, Frances Payne Bolton School of Nursing, Western Reserve University, Cleveland. Edited by Isabel M. Stewart, M.A., R.N. Cloth. $4. Pp. 288. The MacMillan Company, 60 Fifth Ave., New York 11, 1950.

This book, devoted to the administration of schools of nursing, does not attempt to include the administrative functions of the related field of hospital nursing service. It is purposely restricted to educational activities and to the changing pattern of nursing education, which today requires more and more the full attention of those who direct the training of the professional nurse. Beginning with the basic concepts of organization, the author describes in clear and logical manner the present trends in the organization of collegiate and hospital schools of nursing, the relation of the controlling groups, the selection and administration of the faculty, administrative planning for the recruitment and guidance of student personnel, student health, organization of the curriculum, teaching methods, costs and sources of income, school publicity, professional and legislative relations, accreditation of training programs and the qualifications and preparation necessary for the nursing school administrator.

The purpose of the many details of organization and administration described in this book is to aid the directors of individual schools to develop and maintain sound educational programs in keeping with the changing pattern of professional nursing standards. To this end the book will be of valuable assistance to nurses already directing schools and to those who are preparing themselves for administrative duties. It will also be welcomed by hospital directors, physicians and others who may be closely associated with nursing schools in an administrative or advisory capacity. The reader will find a helpful summary at the end of each chapter as well as an extended list of publications for further reference.

Woman's Surgeon: The Life Story of J. Marion Sims. By Seale Harris, M.D. With the Collaboration of Frances Williams Browin. Cloth. $5. Pp. 432, with illustrations. The Macmillan Company, 60 Fifth Ave., New York 11, 1950.

This biography of Marion Sims, the father of modern gynecology, is a fascinating story of a great man written by one of his admirers. The author is a distinguished physician, teacher and investigator as well as a fellow Southerner, who first became interested in Sims when he was only 15 years old. He drove his father, who was a physician, on his daily rounds and listened to the biography of Sims. Dr. Harris' interest in the "woman's surgeon" continued over the years, and this biography is the result of much study and investigation.

Marion Sims was a frail youth born in a well-to-do family. He had no particular interests. His father urged him to study law, and his mother was anxious that the sensitive youth should become a preacher. However, neither of these professions intrigued him, and he studied medicine reluctantly and with little enthusiasm. The first years after graduation were uninteresting and unrewarding. The highlight of this period was his marriage to his childhood sweetheart, who gave him much encouragement in his life's work and remained his faithful partner and helpmate all his life. He finally settled in Montgomery, Ala., where he soon developed an interest in surgery, for which he had much innate ability. His interest was aroused in the wretched complication of vesicovaginal fistula, a common occurrence because of the poor obstetric care. He found this condition in three of his slaves, and these unfortunate women were the willing and trusting victims for 30 attempts at the repair of their fistulas. His persistence, hard work and the use of silver wire for suture effected a cure in one of his patients after 29 failures. Knowledge of his surgical prowess soon spread throughout the South, and he developed a large practice. However, the weather and the recurrence of a chronic ailment for which he had to spend long periods in bed finally decided him to liquidate his interests in Montgomery and move to New York.

The weather and the professional environment worked wonders for Marion Sims. He soon acquired a large practice, because his reputation had preceded him. There were many women, rich and poor, who had sustained childbirth damage or who had other pelvic complications which he could cure. He was a brilliant surgeon and had a special talent for developing new instruments and technics to make his surgery more spectacular. He succeeded in recruiting some of his wealthy patients to help him build a hospital for women's diseases. The Woman's Hospital soon became a mecca for visiting doctors from everywhere. Much of the early history of gynecology was written here by Sims and his early disciples, Emmett, Thomas and Peaslee. He considered the institution his own creation and his home. He soon began the practice of spending longer and longer periods in Europe, and he gained loyal followings in Paris and London. His consulting rooms were filled with international celebrities, including many women from the royal families of Europe. Because of constant arguments with his colleagues and the board of governors of the hospital, his late years were unhappy. In a fit of temper he resigned from the hospital staff, a decision he regretted promptly, but his resignation was accepted. This was a blow from which he never recovered. The author has done a magnificent job in picturing the "woman's surgeon" as a genius in American medicine and yet a human with many human failings. He was selfish; he loved fame and power, and yet he was a kindly man ready to do everything possible for the less privileged. Every physician will enjoy this biography for leisure reading.

Die Wirkungseinheit des Lebens: Eine Einheits-, Spezial- und Ganzheitsbetrachtung der Lebensvorgänge unter normalen und krankhaften Bedingungen. Von Dr. med. Ludwig Seitz. Cloth. 33 marks. Pp. 500, with 54 illustrations. Urban & Schwarzenberg, Thierschstrasse 11, München 22; Meinekestr. 13, Berlin W. 15, 1950.

As indicated in the title, the author has attempted to define the common denominator of all living processes under normal and pathological conditions. He attempts to do for biology what Einstein with his theory of relativity did for physics. That he has not succeeded in reaching this goal is not surprising when one considers how remote from mathematical expression most biologic phenomena are. The author examines, albeit superficially, a wide domain of biologic knowledge, including topics such as the unicellular organism, cosmic and biologic rhythms, the cell as a chemical laboratory, chemical and biomorphological structures, genetics, the gonads, chemohormonal factors in pregnancy, the reflexes, Cushing's disease, the role of the vegetative nervous system in somatic disease, the psyche and a comparison of the modern state and cellular organism. To one philosophically inclined, this range of subject matter will present many points of interest. However, despite the author's constant repetition that all living processes have a common basis, the reader is left with the tantalizing thought that the essence of life cannot be expressed by any simple formula, as promised by the author in his preface. References to the literature are sparse and not critical; the illustrations are schematic drawings which oversimplify and mechanize the physiological principles which they illustrate.

Chemotherapie der Tuberkulose mit den Thiosemikarbazonen. Von Gerhard Domagk. Unter Mitarbeit von C. Arold, et al. Cloth. 60 marks; $14.30. Pp. 405, with 257 illustrations. Georg Thieme Verlag, Diemershaldenstrasse 47, (14a) Stuttgart-O; Agents for U. S. A.: Grune & Stratton, Inc., 381 4th Ave., New York 16, 1950.

This German volume is the result of studies initiated in the hope of establishing a chemotherapy for tuberculosis. Experimental tests were performed exactly and were intended to build a causal therapy for tuberculosis similar to those for other bacterial infections. With the basic acknowledgment of differences between animal experiments and the treatment of tuberculous man, it was recognized that if the semicarbazones, whose specific action was demonstrated in 1946, could affect a human type of tuberculous infection in the highly susceptible guinea pig, such materials in harmless doses might prove useful in the various

forms of tuberculosis in man. While the action of streptomycin is conspicuous in guinea pig tuberculosis, paraaminosalicylic acid (PAS) is poorly tolerated by these animals and is not as acceptable as the semicarbazones, even though it is tolerated better in less susceptible species. Thus the possibility of a causal therapy of tuberculosis exists.

This volume consists of a series of 14 monographs by various authors which to a great extent originally appeared in German periodicals. It is concerned primarily with the results obtained with amithiozone (Tb. 1-698). The initial chapters occupy 141 pages and were written by Domagk, who introduced amithiozone. They include monographs on the bacteriology of the tubercle bacillus, especially its culture and determination, followed by the pathology of tuberculosis in man and, finally, the chemotherapy of tuberculosis, particularly the new semicarbazones. Consideration is given to streptomycin, paraaminosalicylic acid and amithiozone, with the conclusion that amithiozone is second to streptomycin in value and possesses certain advantages, such as length of use and the nondevelopment of resistance by the bacilli. Favorable results from the use of amithiozone are recorded in lupus by Kalkoff, in mucous membrane (upper respiratory tract) tuberculosis by Arold, in lymph gland disease and intestinal tuberculosis by Kuhlmann and Knorr, in urogenital tuberculosis by Boshamer, in bone and joint tuberculosis by Ullmann, in pulmonary tuberculosis by Klee, Melzer, Rühs, Köthe and Jahnke, and Kuhlmann and Lemberger, and in cavernous tuberculosis (local application) by Malluche. In the final monograph, Heilmeyer cites beneficial results from the use of amithiozone in nontuberculous cases, especially chronic rheumatoid arthritis, and records a study of the plasma colloids with this treatment. Though the results cannot be judged to be anything more than beneficial, the monographs disclose an exhaustive study of a new chemotherapeutic compound applied both experimentally in animals and for treatment in man. Although one may not agree entirely with some of the conclusions, the monographs present sufficiently detailed records for the reader to be able to make his own conclusions.

That such a study should emanate from a country decimated so recently by war is astonishing, and yet this volume is doubly interesting in that professional and scientific persons could not be stifled completely, regardless of the political situation. In view of the excellence of the presentation of these monographs and the high quality and durability of materials, even a critical reviewer must conclude that they contain much to stimulate study and to guide future chemotherapeutic possibilities in tuberculosis. The volume presents scientific information and, as such, merits particular consideration for possible corroborative evaluation and productive elaboration.

The Respiratory Function in Laryngectomized Patients. By Rutger Heyden. Acta otolaryngologica, Supplementum LXXXV. Paper. Pp. 76, with 35 illustrations. Lund, 1950.

This magazine supplement, dealing with respiratory function in patients subjected to laryngectomy, is based on an investigation of 44 patients treated for cancer of the larynx during the period 1940-1949 at the Karolinska Sjukhuset in Stockholm, Sweden. The author made spirometric determinations of lung volume and studied respiration with work tests on a bicycle ergometer. Two thirds of the patients examined were able to perform physical work; 58 per cent of them rarely had respiratory infections. The subjects who had undergone laryngectomy appeared to have a somewhat low pulmonary vital capacity.

Biochemical Aspects of Genetics: A Symposium Held at the Westminster Hospital Medical School, London, on 12 February 1949. Organized and edited by E. T. Williams. Biochemical Society Symposia No. 4. Paper 6s; $1.50. Pp. 60, with illustrations. Cambridge University Press, Bentley House, 200 Euston Rd., London, N.W.1; American Branch: 51 Madison Ave., New York 10, 1950.

The symposium, according to one of the speakers, gave a clear demonstration of the connection between genetics and biochemistry in the interpretation of biochemical mutations. The basic concept of the current hypothesis for such mutations is recognition that the genetic abnormality consists of a blocking of a normal metabolic pathway owing to the absence or decrease in concentration of a specific enzyme. Garrod, early in this century, pioneered the work in this field in his study of ochronosis and other inborn metabolic disorders. Discussions on genetic control of biochemical synthesis, chemically induced mutations, gene action and mutation, biochemical genetics of micro-organisms and adaptation, mutation and segregation in the formation of bacterial enzymes are included among the various aspects of the subject.

Le Cancer du corps utérin. Publié sous la direction de P. Chalnot. Avec la collaboration de M. Beau, et al. Questions gynécologiques d'actualité. Pp. 247, with illustrations. L'Expansion scientifique française, 23, Rue du Cherche-Midi, Paris 6e [n.d.].

This is a remarkably complete discussion of all phases of endometrial cancer, with emphasis on newer methods of treatment, by 16 French physicians. The book proceeds logically from an anatomic consideration of the uterus, with emphasis on the lymphatic system, through pathology, possible etiological factors in endometrial cancer, methods of diagnosis, including newer methods of hysterosalpingography (a debatable procedure, but apparently useful in the hands of experts), to treatment.

Emphasis in treatment in the past has been on adequate irradiation, particularly with radium. This is well covered in the present volume. Considerable emphasis is also laid on surgical therapy and on combined irradiation and hysterectomy. The advantages and disadvantages of all procedures are discussed, and statistics drawn from studies made all over the world are presented to show that, in the hands of the authors, combined surgical-irradiation therapy offers the best results. The data on which this conclusion is based must be scrutinized with some care. Whether any series of cases is comparable to any other series of cases is difficult, at best, to determine; and when many of these series are obtained from the literature, it becomes almost impossible to judge their comparability. Despite these statistical drawbacks, it does appear that the French have had good success with a combination of irradiation and hysterectomy in treating endometrial cancer. The data are well presented, and considerable detail regarding procedure is given. Anyone interested in gynecologic surgery or in tumors will find this volume of interest.

Clinical Pathology: Application and Interpretation. By Benjamin B. Wells, M.D., Ph.D., Professor of Medicine, University of Arkansas School of Medicine, Little Rock, Arkansas. Cloth. $6. Pp. 397, with 32 illustrations. W. B. Saunders Company, 218 W. Washington Sq., Philadelphia 5; 7 Grape St., Shaftesbury Ave., London, W.C.2, 1950.

This book is written by a well qualified internist for clinicians, pathologists and medical students. It does not present discussions on technics but offers information on the use and evaluation of laboratory procedures in relation to clinical medicine. Included are chapters on laboratory studies in the surgical and obstetrical fields. Dr. Wells writes, "The practitioner must know at least three things about every laboratory procedure he expects to use: (1) when to use it, (2) how to interpret the results and (3) what technical or physiologic limitations must be taken into account in the interpretation." The procedures covered in the book are available to most physicians. The volume is handy in size and well printed. The views expressed by Dr. Wells are in agreement with those generally held. The book is well written.

The Microscopic Diagnosis of Human Malaria. Part I: A Short Descriptive Atlas of Thick-Film Diagnosis. By John W. Field. Studies from the Institute for Medical Research, Federation of Malaya, No. 23. Paper. $5. Pp. 117, with 81 illustrations by Yap Loy Fong. H. T. Ross, Government Printer, Kuala Lumpur, 1948-1949.

This atlas is for the diagnosis of those types of human malaria encountered in Malaya, including Protozoa falciparum, P. vivax and P. malariae. It includes short accounts of the life histories of the malaria parasites, detailed systematic descriptions of each parasite in lysed, Romanowsky-stained thick films and technical procedures for preparation, staining and examination of the material. It is well illustrated with composite original drawings made with the aid of the microscope and the camera lucida from films stained by Giemsa's or Romanowsky's method. Unfortunately, costs and technical difficulties in Malaya prevented the use of color.

QUERIES AND MINOR NOTES

The answers here published have been prepared by competent authorities. They do not, however, represent the opinions of any official bodies unless specifically stated in the reply. Anonymous communications and queries on postal cards will not be noticed. Every letter must contain the writer's name and address, but these will be omitted on request.

BLOOD PRESSURE OF MORE THAN 300

To the Editor:—An 89 year old white man with arteriosclerosis was seen in 1939 with what was thought to be coronary occlusion, from which he made an uneventful recovery. In April 1950 cardiac decompensation was noted, with a rapid regular rate, edema of the legs, enlarged heart and no murmurs. I could not determine the blood pressure in either arm, nor could I obliterate the radial pulse with a mercury manometer raised to 300 mm. Blood pressure in the legs was not obtainable because of edema; there was no pulsation in the dorsalis pedis artery. Roentgenograms of both arms showed considerable calcification in both brachial arteries. My theory is that these arteries are so calcified that it is impossible to compress them with the blood pressure cuff. Two older internists of wide experience have not encountered this condition, and I am unable to find in the literature anything relative to such a condition. How is blood pressure in the leg properly determined, and what are considered normal values?

M.D., Minnesota.

ANSWER.—It is doubtful whether the failure to obliterate the pulse with a cuff pressure of 300 mm. of mercury is due to the rigidity and incompressibility of sclerotic arteries. One may be almost certain that the systolic tension is actually over 300 mm. of mercury. Levels as high as this, though unusual, are not exceptionally rare. There should be no significant risk in applying greater pressure with a special manometer. Such excessively high levels are not incompatible with the advanced age of the patient.

No mention is made in the query as to any change in note (phase 4) or disappearance of sound (phase 5) as the tension in the cuff is reduced. If one assumes this patient's systolic tension to be somewhere between 300 and 400 mm. of mercury, a diastolic pressure of 150 to 200 should be expected. Anything lower would suggest aortic valve incompetence and regurgitation. The diastolic tension cannot be determined by palpation.

The arterial tension in the legs may be difficult to measure. A wider cuff is needed around the thigh. Sounds in the popliteal space are often very faint, especially when obesity or edema occurs. However, except in cases of coarctation of the aorta, the tension in the legs is 20 to 50 mm. higher than in the arms, when measured with the patient in the recumbent position. If tension is determined with the patient standing erect, the difference is even greater, because of the increased hydrostatic pressure. Readings of tension which are lower in the legs than in the arms are pathognomonic of coarctation of the aorta.

PREOPERATIVE TREATMENT FOR CESAREAN SECTION

To the Editor:—I would like the opinion of (1) anesthesiologists and (2) obstetricians with regard to preoperative medication for cesarean section and especially concerning its use with spinal anesthesia. Is 1/6 grain (0.01 Gm.) morphine sulfate and 1/150 grain (0.44 mg.) scopolamine hydrobromide excessive as preoperative medication if given one hour preoperatively to a 125-130 pound (57-59 Kg.) pregnant woman who has a cephalopelvic disproportion? What are the effects on the infant of these drugs as given preoperatively? Should barbiturates be used?

M.D., New Jersey.

ANSWER.—The anesthesiologist does not feel the need for the preoperative use of morphine and scopolamine when spinal anesthesia is to be used, if the anesthesia is adequate by itself for the obstetric patient in labor. Use of these agents, moreover, is undesirable from the point of view of interference with spontaneous respirations in the newborn. The more cephalopelvic disproportion the patient may have—or in other words, the more prolonged the delivery—the less desirable it is for the infant to be subjected to the effect of morphine and scopolamine hydrobromide. It is true that a barbiturate, used in a small dose, is less undesirable than morphine and scopolamine hydrobromide, yet it is undesirable to have a noticeable barbiturate effect produced in the mother, because the newborn will not breathe as spontaneously as he or she would have done without medication. For elective cesarean section, 50 or 100 mg. of meperidine (demerol®) hydrochloride has proved satisfactory and less depressive for the infant than morphine or barbiturates would be. If a barbiturate is used peroperatively in cesarean section, it is preferable to keep the dose to 1½ grains (90 mg.) of pentobarbital sodium (nembutal®).

CLOTTING TESTS BEFORE TONSILLECTOMY

To the Editor:—Is there any reason to continue the performance as a routine procedure of the clotting and bleeding time tests for tonsillectomy in children?

Lazaro Benavides, M.D., Mexico, D. F.

ANSWER.—Routine evaluation of the clotting and bleeding time prior to tonsillectomy in children may reveal an unsuspected hemorrhagic disease. In hemophilia the coagulation or clotting time is usually prolonged; in the various types of purpura the result of this test is usually normal. In thrombocytopenic purpura the bleeding time is usually prolonged, while in hemophilia it is normal. Probably there are children with a bleeding tendency who do not fall into these categories whom it might be well to detect before operation. Determination of the clotting and bleeding time is the only way in which such tendencies might be discovered before operation.

In most of the leading children's hospitals, the temperature, pulse and respiration rates are noted and a urine specimen is examined prior to operation. Formerly it was also common for specialists to obtain roentgenograms of the chests of the children prior to tonsillectomy in an attempt to ascertain whether an enlarged thymus gland was present, which might result in a fatality from an anesthetic or the operation. This examination has been largely discontinued.

GENERALIZED CONVULSIONS

To the Editor:—On an airplane trip home from my fifteenth college reunion a week ago I felt sleepy as we started to land at Dayton. I woke up to learn from the hostess that I had had "a generalized convulsion which lasted about three minutes, during which 'your pulse rate was about 120.'" A physician boarded the plane, took my blood pressure, listened to my heart, then asked that I be given a dimenhydrinate (dramamine) tablet and ¼ grain (15 mg.) of phenobarbital. He stated that he found nothing abnormal. I felt fine save for the fatigue which one expects after such vigorous conviviality with school mates. I awoke in my own bed about 15 hours after this experience to find my wife in hysterics and a physician neighbor drawing blood from my vein. I felt rested, but was told that I had again had a convulsion. Two neurologists found no evidence of disease. An electrocardiogram showed a 7 second rhythm; I had taken three pentobarbital capsules (0.28 Gm. total) at bedtime, seven hours before the electrocardiogram was taken, and also before the convulsions. I am 37. The only thing in my history worthy of note is that I have a large cranium and I like soft drinks. Laboratory studies show nonprotein nitrogen 34 mg., blood sugar 108 (as the attack subsided) and eosinophils 8 per cent.

M.D., Pittsburgh.

This inquiry was referred to two authorities, whose respective replies follow.—ED.

ANSWER.—It would be a serious mistake to pass off these two generalized convulsions lightly or to attribute them to some relatively innocuous agent such as pentobarbital. Pentobarbital, even in fairly large doses, does not give rise to convulsions. The situation demands thorough investigation from a neurological and neurosurgical standpoint. The inquirer should place himself under the care of some neurologist or neurosurgeon and follow his recommendations.

ANSWER.—Although the 8 per cent eosinophil count is somewhat suggestive of the presence of allergy and the episodes presented have been on rare occasions claimed to be due to allergic causes, it would be presumptuous and hazardous to consider allergy the most important cause. It is decidedly more important that this condition be investigated from the neurologic, psychogenic, vascular or other medical approach.

ELECTROSHOCK TREATMENTS

To the Editor:—A patient had a series of electroshock treatments concurrently with subshock doses of insulin. She has heard that this form of treatment shortens a person's life and causes permanent physical damage. Is there any evidence to disprove this belief?

M.D., Arizona.

ANSWER.—Numerous brains of both man and animal have been examined after electroshock treatments, and there has been no significant change found in the architecture. The same is essentially true with insulin shock, particularly the subshock variety. Occasionally in either, oftener with insulin, there are

a few changes in and about the blood vessels, some glial changes, but no significant permanent damage.

Fractures of bones, essentially mild compressions of the vertebrae and rupture of muscles do occur, but they, too, are inconsequential. When the bones are osteoporotic the vertebral column should always be examined roentgenographically before treatment. Treatment may be pursued with the use of curare or curare-like substances to avoid the violent convulsion.

The electroshock treatment appears to have no effect on a normal heart. Patients with severe myocardial damage have been treated successfully without any untoward effect on the heart. Here the decision depends on the circumstances. When the patient is literally thrashing himself to death, it becomes a life-saving, hence justifiable, risk. When a patient known to have cardiac damage develops a psychosis which is resistant to all conservative therapy and shock treatment is necessary, treatment may go on, with curare used as mentioned above or a sedative like a barbiturate given intravenously. This moderates the convulsion. Curare supervised by a competent anesthetist is preferred. This, of course, means having available a mechanical respirator, and, if necessary, neostigmine. Occasionally death occurs from myocardial infarction.

After intensive electroshock treatment the patient has a sense of memory loss. The actual period of treatment frequently is an island of blankness. Spontaneous memory seems to be more affected than that of learned didactic material; yet after a few months the patient seems to recapture everything but the period of treatment. All except those who had previous organic brain damage are able to return to their pre-illness status, or occupation, if the electroshock was effective. Subshock with insulin combined with electroshock adds no further changes except that the deep confusion often associated with intensive electroshock treatment comes on more slowly and clears more rapidly.

EPILEPSY AND OSTEOGENESIS IMPERFECTA

To the Editor:—A 9 year old boy has had osteogenesis imperfecta of the congenital type. He sustained his first spontaneous fracture at the age of 9 months and since then has had eight more fractures. The last of these, a year and a half ago, followed sufficient trauma to cause the fracture of a normal bone. We believe that this condition is now in remission. In addition, from 1944 to 1947 the child had 17 grand mal type convulsions, some following febrile illnesses. He has been studied at a reputable clinic, and it was considered that he suffered from idiopathic epilepsy. Electroencephalograms of the father showed an epileptic pattern, though he has never had frank convulsions. The paternal grandfather suffered from some type of convulsive disorder. There is no other history of spontaneous fractures among either parents or grandparents, nor have I seen any other family members who had blue scleras. The parents of this boy want another child. They have received conflicting advice from several sources. What is your recommendation?

M.D., South Carolina.

Answer.—Many pedigrees are on record showing a high incidence of osteogenesis imperfecta among both close and distant relatives; in some families it has appeared in as many as five generations. Epilepsy is not always inherited. In the case just cited, however, it would appear to be familial in origin. Again, as in the case of osteogenesis imperfecta, there are many family trees on record which reveal numerous cases of epilepsy among blood relatives. The existence of either of these diseases alone should be a sufficient contraindication to future childbearing.

HIRSUTISM

To the Editor:—A woman aged 35 complains of having to shave twice daily because of a beard of coarse hairs, increasing since onset six years ago. There are no other masculinizing signs, such as change of voice, temperament, enlargement of the clitoris or male distribution of pubic hair and no menstrual changes. The patient blames her hirsutism on progesterone, of which she received a total of three injections of 10 mg. each at monthly intervals prior to the appearance of the hair. Can you refer me to scientific studies which confirm or disprove this contention?

M.D., California.

Answer.—There are no data in the literature which suggest that the administration of progesterone causes hirsutism. The patient should be carefully studied to determine whether she has a masculinizing tumor. The simplest laboratory test is a determination of 17-ketosteroid excretion in the urine. If the value is within normal limits, it is probable that no masculinizing tumor is present.

REFRACTION DURING PREGNANCY

To the Editor:—Should a refraction of the eyes be postponed merely because a patient is pregnant?

Gilbert C. Norton, M.D., Endicott, N. Y.

Answer.—There are no significant ocular changes in normal pregnancy that influence errors of refraction. Refraction should not be postponed merely because a patient is pregnant.

POOR LACRIMAL DRAINAGE IN INFANT

To the Editor:—A male infant, 14 months of age, has had faulty drainage of tears in his right eye since birth. An ophthalmologist has probed his lacrimal duct twice, with apparently no results. What is recommended to correct this condition?

Abe L. Feuer, M.D., Dallas, N. C.

Answer.—A special form of lacrimal disease is occasionally seen in infants after the first few days of life. If development of the lacrimal duct is not complete at birth, the condition soon manifests itself by epiphora and slight mucopurulent discharge from the eye. The fact that the conjunctiva is not inflamed is usually sufficient to establish the diagnosis. The lacrimal sac may become distended from retention of tears and secretion, and sometimes dacryocystitis may result. The condition is often self limited, or one may relieve it by pressing the sac and forcing its contents into the nose, thus establishing the patency of the duct. This type of obstruction, which is an epithelial plug or membrane, does not tend to reform. If this method is not successful, syringing the passages or passing a lacrimal probe will usually relieve it. Frequently only one probing is required but several probings may be necessary.

FATIGABILITY

To the Editor:—A white man, aged 48, has a low systolic blood pressure, namely, 90/65. He has no complaint except fatigability. The blood pressure several years ago was 110/70. He has been taking 5 mg. of *d*-amphetamine sulfate in the morning and at noon without any effect on the blood pressure. What else would you recommend? Laboratory tests revealed no abnormalities.

M.D., Wisconsin.

Answer.—This patient is fortunate. With blood pressure at such a level his statistical chances of outliving those with pressures slightly above average normal are good. His fatigability is almost surely not due to the height of the arterial pressure and probably indicates that the patient requires more frequent, if less prolonged, periods of rest. No medication is required, but the patient must be convinced of his superior rather than inferior vascular status.

WHITE FINGER NAILS SINCE BIRTH

To the Editor:—The nails of an 18 year old girl have been white on the tip and (the protruding portion) since birth. Can you explain this?

M.D., Kentucky.

Answer.—The young woman apparently has leukonychia. This condition appears most often in one or more nails in the form of white punctate or transverse striae, but occasionally the entire nail may be involved or a portion of it, and the involvement may be symmetric or asymetric. Usually the finger nails are affected, but the condition has been observed also in the toe nails. The whiteness is likely due to imperfectly cornified cells with the presence of granules of keratohyalin, due to a functional disturbance of the ungueal matrix, trophic disturbances or even trauma. Trauma, as from manicuring, is frequently blamed for leukonychia, but congenital-familial cases have been observed. In many cases the cause remains unknown.

ODOR OF URINE AFTER EATING ASPARAGUS

To the Editor:—Eating of asparagus seems to be followed by the excretion of malodorous urine. What causes this odor? Some have said that asparagus "purifies" the kidneys. I cannot understand such reasoning.

Irving I. Crouse, M.D., Buffalo.

Answer.—The odor which appears in the urine after the ingestion of asparagus is due to the volatile sulfur compound methylmercaptan, which is formed as a breakdown product of the asparagin found in asparagus. This odor may persist for 12 to 20 hours and has been mainly responsible for the belief in the diuretic properties of asparagus. However, there is at present no sufficient reason for the belief that asparagus is of value in practical medicine. Because of its purin content, it is especially contraindicated for patients with gout.

LOW DIASTOLIC PRESSURE IN YOUNG PATIENTS

To the Editor:—In Queries and Minor Notes in *The Journal* of Oct. 7, 1950 (page 512) the cause of very low or zero diastolic pressure is discussed. I should like to add a point that may explain many of such readings. While one is listening for the disappearance or change of the systolic sound while the pressure cuff is being deflated, pressure with the bell or diaphragm of the stethoscope over the brachial artery will often cause a partial occlusion of the blood vessel. This has the same effect as a partially inflated cuff. One will then hear the pulsation of the blood even when the air cuff is completely deflated. This is particularly true in young persons or those with elastic arterial walls. Therefore, when one obtains a very low diastolic reading, merely easing up on the pressure with which the stethoscope is applied to the artery will result in complete disappearance of a "low diastolic pressure."

Isadore Pitesky, S.B., Medical Student, University of Illinois, Chicago.